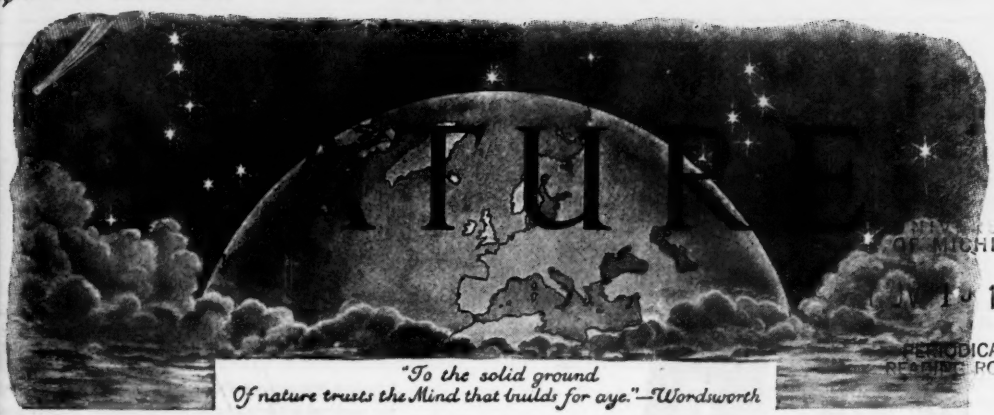

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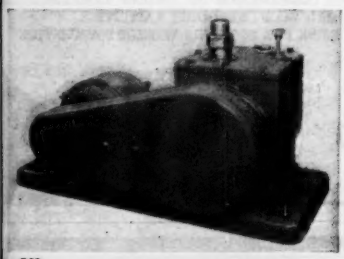

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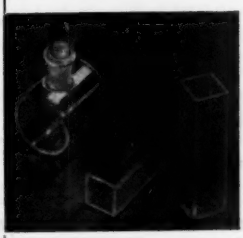

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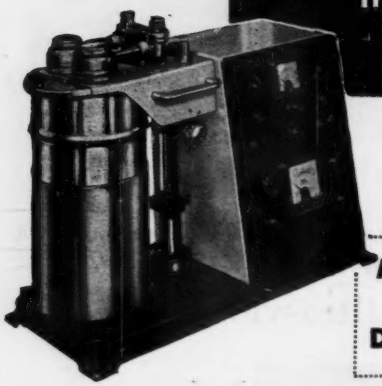

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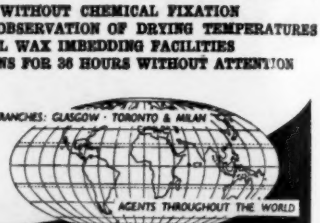

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CONTENTS

	Page
Scientific and Industrial Research in the Universities	943
Geneva Conference on the Peaceful Uses of Atomic Energy. By Dr. T. E. Allibone, F.R.S.	944
Science in Progress. By Dr. W. L. Sumner	946
The Natural History of Space Perception.	946
New Techniques and Applications in Molecular Spectroscopy. By Dr. R. Schnurmann	947
Chemically Induced Neoplasms in Fungi. By Prof. P. T. Thomas, Dr. H. J. Evans and D. T. Hughes	949
Education and Productivity in Under-developed Areas. By P. C. C. Evans	951
Physiology in the Polar Regions. By Dr. O. G. Edholm.	954
Metal Fatigue in Theory and Design. By Dr. A. J. Kennedy	957
Obituary :	
Prof. John Garstang. By Prof. H. W. Fairman	959
News and Views	960
The Direction of Research Establishments. By E. S. Hiscocks.	964
International Society of Bioclimatology and Biometeorology. By M. J. Delany and F. L. Waterhouse	966
Yeast in Industry. By Dr. C. Rainbow	966
Free Radicals: Symposium of the Chemical Institute of Canada. By Dr. B. A. Thrush	968
Inspection of Industrial Pollution in Britain: Report for 1955	970
Bird Semantics	970
Pan Indian Ocean Science Congress	971
Methods for the Study of Human Relations in Industry	971
Plant Growth-Regulating Activity in Certain Carboxylic Acids not possessing a Ring Structure. By Dr. C. H. Fawcett, Prof. R. L. Wain and Dr. F. Wightman	972
Inhibition of Plant Cytochrome Oxidase by Bicarbonate. By Gene W. Miller and Prof. Harold J. Evans	974
A Cytological Study of the Neurones of *Patella vulgata* by Light and Electron Microscopy. By Dr. Dennis Lacy and Robert Horne	976
Role of Oxygen in modifying the Radiosensitivity of *E. coli* B. By Tikvah Alper and Dr. P. Howard-Flanders	978
Letters to the Editors:	
Output of Sympathin from the Spleen.—Prof. G. L. Brown, C.B.E., F.R.S., and Dr. J. S. Gillespie	980
Autoradiography of End-plates with Carbon-14–Calabash–Curarine I and Carbon-14–Decamethonium.—Dr. P. G. Waser and N. Lüthi	981
Globulins in the Chicken Egg-White.—Dr. Marie Kaminski	981
Coagulase Activity *in vivo*.—Douglas D. Smith and Dr. J. M. Johnstone	982
Anaerobic Uptake of Glucose *in vitro* by the Isolated Rat Diaphragm.—Dr. P. J. Randle	983
Heat Changes during the Clotting of Fibrinogen.—K. Laki and C. Kitzinger	985
Cell Membranes and Morphogenesis.—M. S. C. Birbeck and Dr. E. H. Mercer	985
A New Method for the Identification of Biochemical Mutants of Micro-organisms.—R. Holliday	987
The Snail's Foot as a Langmuir Trough.—Dr. D. F. Cheesman	987
Influence of Freezing-rate on the Denaturation of Cold-stored Fish.—R. M. Love	988
Protective Action of Vitamin B_{12} in Experimental Liver Injury.—D. K. Kasbekar, Dr. D. V. Rege and Prof. A. Sreenivasan	989
Lability of Intramitochondrial Components in Experimental Liver Injury.—D. K. Kasbekar and Prof. A. Sreenivasan	989
Diphenylhydantoin and Brain-Levels of 5-Hydroxytryptamine.—Prof. D. D. Bonnycastle, Dr. M. K. Paasonen and Dr. N. J. Giarman	990
Shikimic Acid in Apple Fruits.—Dr. A. C. Hulme.	991
Physiological Control of Population Growth.—W. K. Whitten	992
Influence of Light on Sporulation of Brewing Yeast.—Dr. W. F. F. Oppenoorth	992
Autolytic 'Protoplast' Release in *Bacterium coli*.—Dr. Peter Mitchell and Jennifer Moyle	993
Application of Large Volumes in Small Spots on Paper Chromatogram Strips.—W. J. van Gulik	994
Chromatography of Insulin on Calcium Phosphate Columns.—W. Dickinson	994
An Improved Method for the Preparation of Sialic Acid or Acetylneuraminic Acid.—Yoshiharu Saito	995
New Analeptics and Hypnotics related to the Barbiturate Antagonist, 'Bemegride'.—T. C. Somers	996
Use of the Infra Red Spectrum to distinguish Bridging from Terminal Thiocyanato-S-Groups in Co-ordination Compounds.—Dr. J. Chatt and L. A. Duncanson	997
Vapour Pressures of Some Disperse Dyes.—Dr. R. S. Bradley, C. L. Bird and F. Jones	998
Oxidation-Reduction Reactions of Metal Salts in Non-aqueous Solvents.—Dr. L. H. Sutcliffe and J. Walkley	999
Crystal Structure of 1:2–Benzanthracene.—P. H. Friedlander and D. Sayre	999
Absorption of Oxygen and Carbon Monoxide by Barium Alloy Getters.—R. N. Bloomer	1000
Change in Surface Area of Anthracite on Heat Treatment.—P. L. Walker, jun., and Irwin Geller	1001
The Golgi Apparatus and Secretion of Enzymes in Peptic Cells of Rabbit.—Dr. Tohamy A. Moussa	1002
Relationship between Blood Concentration and Environmental Salinity in *Palaemonetes varians* (Leach).—B. Lofts	1003
A Spiral 'Valve' in the Hepatic Portal Vein.—H. de C. Baker	1003
Life-History of *Phyllodistomum simile* Nybelin.—Dr. J. D. Thomas	1004
Meiosis without Chiasmata in *Periplaneta americana*.—Dr. G. P. Sharma, Ram Parshad and Miss Prem Sehgal	1004
Crossing-over in *Drosophila willistoni*.—Dr. Bruno Battaglia and Dr. L. C. Birch	1005
Chromosomes of the Cultivated Mushroom.—H. J. Evans	1005
Dormancy of Seeds of *Phalaris arundinacea* and *Phalaris tuberosa*.—P. B. Vose	1006
Differences in Social Aggregation in Two Species of Locust.—Dr. Peggy E. Ellis	1007
"Lucubratory Biochemistry."—Prof. Felix Haurowitz: Prof. F. G. Young, F.R.S.	1008
A Word Common to the Natives of Alaska, Canada, Greenland and Brazil.—Dr. Vilhjalmur Stefansson	1008

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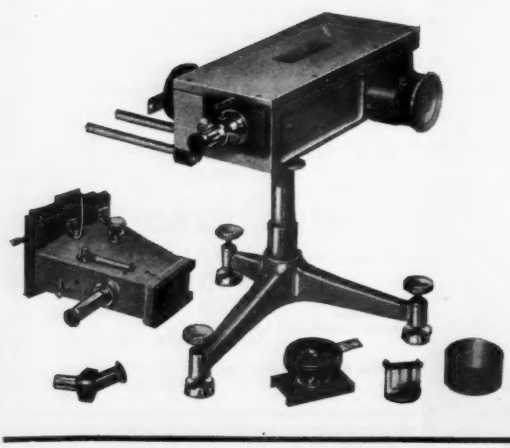

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SCIENTIFIC AND INDUSTRIAL RESEARCH IN THE UNIVERSITIES

THE problem of finding the money for carrying out research in university departments of science and technology in Britain has been growing steadily more acute, and there has been considerable discussion in recent months which has served to show both its magnitude and the difficulties inherent in meeting it. Prof. Samuel H. Beer has produced a timely little book* which demonstrates that something in the way of positive, constructive thinking is required if we are not to drift in some emergency into a situation which will endanger both the autonomy of the universities and the balance, or even the conduct, of research in general.

Prof. Beer is concerned simply with the role of the Treasury as co-ordinator of financial and economic policy, and in the first place he is impressed with the Treasury's lack of positive powers of command. But the picture he gives of the way in which the Treasury is able in practice to enforce effectively the priorities of Government policy indicates the importance of institutions or activities subject to Government control, such as the University Grants Committee or the Department of Scientific and Industrial Research, being ready and able to present a clear and reasoned argument for their needs which can be fully justified by reference to national needs. The Treasury does possess some powerful sanctions; but supporting these is a 'structure of influence' that enables it to carry out most of its wishes by persuasion. This is the important factor where such activities as research and institutions like the University Grants Committee are concerned.

In this attempt to understand the relations of the Treasury with the other great Departments of State, Prof. Beer notes a strong tendency to reach agreement at the official level which has roots in the corporate life of the Civil Service. It has frequently been suggested that one of the reasons for the smooth working of the University Grants Committee system is that the senior Civil servants concerned have themselves a university education and outlook, and a like factor can operate also in relation to Ministerial collective responsibility. Where this operates and Ministers know their own minds, the co-ordination works smoothly. Officials are able to go beyond the mere departmental view and anticipate probable decisions at Ministerial level. In its absence, however, and where Ministers cannot agree, the whole process may break down.

But Prof. Beer's tribute to the efficiency of Civil Service administration at the highest level does not deal with one vital point. If he is correct in his view that the power of the Treasury resides largely in the tendency to agreement proceeding from the professional standards of the Civil Service and from the structure of Britain's executive power, that of itself affords no assurance that the right agreements will be reached. It says nothing as to whether the Treasury is properly equipped for reaching right decisions in matters of planning, or as to whether the standards of efficiency which it applies in such matters as research, for example, are in line with modern conceptions and practice. Tendencies to agreement at any level will not ensure sound decisions unless there is clear understanding on all sides of the nature of the problem, including the scientific and technical factors involved.

Prof. Beer's little treatise is thus less reassuring than appears at first sight, and by implication his exposition of the nature of Treasury control reinforces all the arguments for ensuring that the future administrator has an adequate understanding of the nature of the scientific and technical problems in the situations and problems he will have to confront. It indicates, too, the value of making the fullest use of those scientists who possess administrative ability, and it should remind the scientist and technologist of the importance of taking care that the nature of their work and the conditions required for its effective pursuit are clearly explained to those from whom the means for its prosecution are drawn.

This question of public relations is of vital importance both in relation to university research, which clearly is not easily separated from the activities of the universities as a whole, and in relation to the nation's general research organization. Understanding and foresight are essential if the delicate balance is not to be disturbed, and waste of public resources through some ill-judged and short-sighted economy avoided. It might well be that, as was urged in the debates on the Department of Scientific and Industrial Research Bill in the House of Commons, a senior Minister, provided with an adequate staff, and charged with the responsibility for co-ordination and prosecution of our scientific and technical effort, could do something to improve the present position. Apart altogether from the question whether any one man could adequately meet the demands which such a responsibility would make upon him, he could only hope to do so under exactly the conditions which Prof. Beer lays down for effective Treasury control in general, and presupposing a wide degree of understanding of the scientific and technical factors on the part of those with whom he is called upon to deal.

What needs to be emphasized is that a wide degree of public understanding is essential before we can hope to arrive at the most efficient and appropriate structure for the administration of Britain's research effort. To some extent recent debates in Parliament have assisted that process; but there is still much that the Parliamentary and Scientific Committee, for example, could do in this direction. Further, if Britain is indeed lagging behind the United States in expenditure on research, as the preliminary estimates from the survey made by the Department of Scientific and Industrial Research suggest, the situation is not

* Treasury Control: The Co-ordination of Financial and Economic Policy in Great Britain. By Prof. Samuel H. Beer. Pp. ix+138. (Oxford: Clarendon Press; London: Oxford University Press, 1956.) 15s. net.

likely to be improved by administrative action done in the absence of such wider understanding. A change in the climate of opinion may be an essential for the necessary financial provision to be forthcoming and for the effective presentation of research. As Sir Harold Himsworth pointed out at the Home Universities Conference held last winter, neither universities nor research organizations alone are able under modern conditions to carry the whole breadth and depth of the research required for the support and development of modern society. Both must contribute, and as partners in the full sense of the word. Whatever the future relation between them and between them and the Government, nothing should be done which impairs the independence of the universities and their freedom to develop according to their own inspirations. Prof. H. W. Melville had referred during the Conference to the possibility that the Department of Scientific and Industrial Research might provide a means of redressing the balance of fundamental research when it was found that certain subjects were neglected in the universities. It would be undesirable for any Government department to induce, by direct action, the universities to undertake investigations which they do not at present pursue, even though such researches might be in the national interest; but Prof. Melville thought that either by undertaking the investigation itself or by adopting the unit system by which the Medical Research Council and the Agricultural Research Council at present operate in the universities, the Department of Scientific and Industrial Research could exert a marked influence.

Here we see at once how important it is that there should be a full understanding of the nature of the Department's work and a balanced view of the country's needs, without which the necessary resources are unlikely to be forthcoming. Moreover, that applies equally to Sir Harold Himsworth's point about the access of individual universities to specialized facilities which they need but which they do not possess, and which it would be undesirable and uneconomic to duplicate in every university, particularly as they are available in many research institutes and stations. This is a particular aspect of the problem of the proper association of existing major research institutes and establishments with the appropriate university departments that can affect very considerably the return which the country receives from its expenditure on research and on the universities.

These are some of the problems which the universities, the research councils and research associations should be considering, and they determine the value which is received for expenditure on research. Moreover, while, as has been emphasized, appropriate solutions are unlikely to be found or at least applied in the absence of a wider and fuller public understanding of what is involved, that public understanding could simultaneously help to remove the most serious weakness to which the survey described by Mr. E. Rudd in a paper before Section F (Economics) at the recent Sheffield meeting of the British Association points—the much smaller expenditure on research by industry in Britain. If industry is to increase its own effort, still more to increase those benefactions to university research which can decrease the risk of excessive dependence on government support or contract research, it will only be in the light of fuller understanding of the nature of research and of the contribution which scientific advance can make to industrial development and efficiency. While the magnitude of Britain's effort in research and development may well be open to inquiry, and the structure of the national organization for research requires critical thought and inquiry, the overriding need is for fuller public understanding of what is involved, and of the dependence of our industrial effort not only upon research but equally upon technological and technical education.

GENEVA CONFERENCE ON THE PEACEFUL USES OF ATOMIC ENERGY

Proceedings of the International Conference on the Peaceful Uses of Atomic Energy

Held in Geneva, 8 August–20 August, 1955. Vol. 15: Applications of Radioactive Isotopes and Fission Products in Research and Industry. Pp. viii+327. 7.50 dollars; 54*s*.; 32 Swiss francs. Vol. 12: Radioactive Isotopes and Ionizing Radiations in Agriculture, Physiology, and Biochemistry. Pp. ix+553. 9 dollars; 63*s*.; 39 Swiss francs. Vol. 10: Radioactive Isotopes and Nuclear Radiations in Medicine. Pp. x+544. 8 dollars; 57*s*.; 34 Swiss francs. (New York: United Nations; London: H.M. Stationery Office, 1956.)

IT was said, I think first by Robert Oppenheimer, that the increase of knowledge as the result of the widespread use of radioactive tracer elements in research might bestow greater benefits on mankind than would result from the mere supply of energy from uranium fission. These three volumes present a very comprehensive review of what has been achieved thus far with tracer elements and with massive doses of radiation derived either from elements such as cobalt, left in a high-flux reactor for a long time, or from fission products. The nuclear power industry will yield tons of fission products a year in a decade, and scientists have been searching for possible uses of the thousands of millions of curies of radiation which will be available as a by-product. Before the end of the century, fission-product radiation could sterilize far more food than the population using the related nuclear energy could consume: such is the magnitude of the new source of energy.

Research with radioactive tracer elements was initiated more than forty years ago by Prof. G. de Hevesy, who was present at Geneva. Many papers on a large number of subjects have their origin in his work. Great strides have been made in chemical analysis by irradiation of samples in a neutron flux of $10^{12} n/cm.^2/sec.$; many impurity elements can then be detected in concentrations of one part in a hundred million, and for a few elements the sensitivity is a thousand times greater than this. Trace impurities can seriously affect the semiconducting characteristics of germanium and silicon,

and both have benefited by activation analysis; it also offers great advantage over other possible methods when the impurity element has chemical properties similar to the host element. Most of the papers on this subject are indicative: the authors recognize that the subject, although old, is far from fully developed, and results are offered as a guide. Tracers have been used in the study of the mechanism of chemical reactions, the function of catalysts, absorption and desorption, and in many metallurgical problems. When a radioactive metal diffuses into another metal, the influence of the grain boundary on diffusion-rates can be studied precisely.

The technological importance of isotopes is exemplified in the very large number of papers which report the use of isotopes as gauges, gauges for thickness measurements ranging from 0·0001 in. for inks, paints and electroplating up to 2 in. of steel and 15 ft. of snow. Locating gauges have been used in fluid dynamics for indicating interfaces, the degree of mixing of gases, of liquids and of solids; flow gauges to follow the movement of silt in river beds and sand in harbours; and density gauges for the manufacture of cigarettes and for liquids in pipe lines. In the study of wear and the influence of lubrication on wear, isotopes have been widely used; recent Soviet work is reported on this subject, and there is an extensive survey of the use of isotopes in the steel-making industry of the U.S.S.R.

Strong sources of radiation can replace X-ray tubes for certain radiographic purposes. Thousands of curies of iridium, emitting 600-keV. γ-rays, are used for boiler weld radiography, and in time cæsium-137 separated from other fission products will doubtless more than satisfy all possible needs for γ-rays in this energy-range. Thulium, emitting γ-rays of 84 keV. energy, has been made up into extremely portable X-ray units for field use—again, thulium may possibly be superseded by the fission product xenon. Cobalt-60 has practically ousted radium in the γ-ray energy-range of 1–2 MeV. for medical therapeutic use.

The role of fission products in human history lies in the unforeseeable future. At present we see the use of γ-rays to break chemical bonds and polymerize and cross-link many molecules such as polythene and rubbers; but only a beginning has been made. The sterilization of foods and pharmaceuticals has been studied for years with some success; but a ten-year summarizing paper still speaks very cautiously of the future possibilities of the widespread use of fission products; the direct conversion of radiation into electrical energy appears to have little future except for special restricted applications.

Those scientists who do not work in the life sciences will enjoy many fascinating papers in Vols. 10 and 12, on radioactive isotopes and nuclear radiation in medicine and in agriculture, physiology and biochemistry. There are lengthy accounts from many countries of the use of tracers in agriculture, especially in the study of root and leaf fertilizers, plant growth, and the speed of chemical processes taking place in plant life. Labelled phosphate fertilizers are now made by the ton, so great is the demand for agricultural research, and accurate information on the absorption through the leaves may revolutionize crop fertilization. Isotopes led to the discovery of extensive root-grafting of trees—a forest must be considered as a united community rather than as a collection of individuals—and the danger of fungus invasion by the root system is thus more obvious. It is disquieting to learn that the weedkiller 2-4-D can be absorbed by edible plants, and it is clearly important, as one review article points out, to establish that such compounds have no effect on the consumer—man or animal.

Mutations induced by irradiation are being studied in the radiation fields at Brookhaven, and in Norway, the U.S.S.R. and elsewhere. It is not easy to judge whether really important mutants have been discovered yet—mutants which have not already been developed by intensive breeding, the rust-resistant oats, the improved peanuts, the more erect variants of barley, etc. Improvements are expressed by writers only in terms of small percentages, and one wonders what commercial advantage red carnations grown on a white carnation stock will have. But patience is needed, and progress is being made on a wide front. Among the valuable uses of intense sources are to be included the eradication of the screw worm fly by sterilization of large numbers of male flies with doses of 7,500 roentgens; in this way the island of Curacao has been freed from this damaging pest. The treatment of potatoes and carrots with a similar γ-ray dose completely inhibits sprouting and growth for a year.

Pavlov's plea for an exact knowledge of the fate of food within organisms is likely to be answered now that tracer elements are in wide use. It comes as a surprise to learn that calcium is constantly passing from blood to bone and back again. For example, one writer reports that 99 per cent of labelled calcium is deposited in the bone within one day of ingestion, and the amount of calcium exchanged to and fro is a hundred times the amount retained for growth. The speed of some reactions is very great; thus, within ten minutes of adding chlorine ions to the blood, equilibrium is established between plasma and red cells. Photosynthesis is yielding up some of its mysteries with the aid of carbon-14, and many papers are devoted to this huge subject. At first, says one contributor, it seemed that the use of isotopes would solve most of the more difficult problems of animal nutrition; many answers have been supplied by isotopes, but not the simple ones which were expected, and a more complex state of affairs has been uncovered.

Apart from an extensive use of tracers in medical research, medical diagnosis and therapy have benefited greatly from the ready availability of radioactive sources. Diagnosis by iodine uptake of the malfunctioning of the thyroid gland is one of the oldest. More recently, radioactive iodine and arsenic have been used for location of metastases of tumours; where great accuracy of location is required, as for the location of brain tumours, the positron-emitter arsenic-74 is used, and two scintillation counters placed on opposite sides of the head record coincidence counts if the two γ-rays which are emitted simultaneously and in opposite directions when the positron decays pass through the counters. Radioactive iron is used in diagnosis of diseases affecting bone marrow, and radiochromium or radiosodium is used in the study of the circulation of the blood. Many more diagnoses with radioactive elements are in the research stage and show great potential value, although few are ripe for routine laboratory use; the future for accurate diagnosis appears to the layman to be far brighter than the past has been.

Radiation therapy has benefited by the large use of strong radiocobalt sources in place of radium

bombs emitting a far lower intensity of radiation. Cæsium-137, which emits a rather softer radiation of 660-keV. energy, is just becoming available from fission separation plants and will supply all conceivable needs of therapy in a decade or so. Iodine selectively absorbed can be used in large doses for therapy, and so can phosphorus; gold in colloid form has been injected locally, and a new technique involves the irradiation of intravenously injected boron in a slow-neutron beam emerging from a reactor.

Vol. 10, on the use of nuclear radiations in medicine, is one of the most remarkable volumes from the Geneva Conference, and one of the most inspiring.

T. E. Allibone

SCIENCE IN PROGRESS

Science in Progress

Edited by George A. Baitsell. Ninth Series. (The Society of the Sigma Xi devoted to the Encouragement of Research in Science. Sigma Xi National Lectureships 1953 and 1954.) Pp. xviii+343. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1955.) 6.50 dollars; 52*s.* net.

THIS new volume, the ninth in the series of "Science in Progress" publications, which began with Vol. 1 in 1939, continues the firmly established function of the series: the presentation in permanent form of authoritative reports of research in both pure and applied sciences. George A. Baitsell has produced an engaging and varied mixture of topics. It would be unfair to say that the accounts are couched in popular language; but generally they are not loaded with heavy technicalities.

A reader with a grammar school knowledge of chemistry and biology will find Kenneth V. Thimann's paper on the physiology of growth tissues easy to understand; but a specialized knowledge of mathematical aerodynamics is necessary to comprehend fully the second part of D. B. Steinman's account of the stability of suspension bridges. The first part of this chapter makes exciting reading. It tells of the unexpected destruction of suspension bridges which were able to absorb energy from winds of quite moderate velocity and sustain themselves in oscillation. An example occurred in late 1940 when the Tacoma Narrows Bridge at Paget Sound, new only four months previously and built at a cost of six and a half million dollars, was destroyed. The oscillations of the bridge increased to destructive amplitude until the main span broke up and dropped into the water 208 ft. below. The problem concerning this has been solved both theoretically and practically.

In a forty-page chapter, Lawrence M. Snyder, professor of genetics in the University of Oklahoma, gives a summary of the present knowledge of human heredity, with special reference to clinical problems, some of which are of rare occurrence. This is followed by a discussion by Curt Stern, of the University of California, on the cellular physiology of differentiation by means of which an embryonic cell is transformed gradually and in the end, usually irreversibly, into a differentiated cell. His investigations, which were suggested by the arrangement of bristles on the fruit-fly, carry the knowledge of this topic further forward; but in general the nature of the mechanisms of differentiation is still obscure.

E. J. Krans, of Oregon State College, is the author of a chapter, easy to read but thoroughly sound, on the significance of ergocrines in agricultural practice. In this well-illustrated chapter the author considers the effects of the synthetic plant-hormone substances both as plant-growth stimulants and as herbicides. The processes of visual excitation provide an instance of a biological problem which is investigated on the molecular level. George Wald, of Harvard University, has given a thorough, clear and authoritative account of the biochemical and physical properties of retinal molecules and their function in seeing.

Lee E. Farr, of the Brookhaven National Laboratory, presents a paper on the impact of nuclear science on medicine. This is by no means well-trodden ground, for, among other important matters, he gives accounts of the effects of radiation on immunity mechanisms, the use of carbon isotopes for exploring the methods by which amino-acids are converted to protein in living tissues, and the radiation of brain tissue. Felix Bloch, of Stanford University, gives an account of the apparatus and methods used for investigating nuclear magnetism, which is a model of clarity and simplicity in exposition. In particular, the technique is applied to a detailed study of molecular structure.

Two other chapters maintain the high quality of the others: transistor physics, by William Shockley (Bell Telephone Laboratories); and colour and chemical construction, by Wallace R. Brode (National Bureau of Standards, Washington, D.C.). Although these two subjects have been covered adequately in papers and articles published in Britain, the American method of presenting the material should prove to be instructive.

The book is a handsome volume, well printed and illustrated, on good paper, and worthily bound.

W. L. Sumner

THE NATURAL HISTORY OF SPACE PERCEPTION

The Child's Conception of Space

By Jean Piaget and Bärbel Inhelder. Translated from the French by F. J. Langdon and J. L. Lunzer. (International Library of Psychology, Philosophy and Scientific Method.) Pp. xii+490. (London: Routledge and Kegan Paul, Ltd., 1956.) 42*s.* net.

THIS is an important book, probably the most notable of the long series of similar studies on child development which have come from Prof. Jean Piaget's laboratory. In it the developing powers of the child to manipulate and talk about objects in space are explored and systematically described. It is typical of Piaget's approach that the course of the investigation seems to have been, in part at least, determined by purely logical considerations. Thus the reader moves from topological space through projective space into Euclidean space. Consequently, the whole account has an orderliness that is often missing from child studies carried out elsewhere. On the other hand, the empiricist might complain that Piaget and Inhelder's data are used for illustrating rather than proving an essentially deductive set of theories and that the order is imposed, not discovered.

Since this line of criticism is perhaps the only one to which these admirable studies seem open, it may be considered further. To begin with, the detailed statistics now regarded as desirable in Britain and America are nowhere presented by Piaget and Inhelder. To be sure, one paragraph in Part 2 begins promisingly : "These experiments were carried out on 100 children, 21 between 4 and 6 : 6 years, 30 between 6 : 7 and 8 years, 33 between 8 and 9 : 6 years and 16 between 9 : 6 [should it be 9 : 7 ?] and 12 years", but in the subsequent text no attempt is made to relate the developmental stages in space perception to any given number of children of a particular age. It is clear, however, from the whole nature of this study that Piaget and Inhelder are primarily concerned with what follows what, and are not particularly interested in the precise age at which the different stages occur. If anyone wishes to construct a developmental quotient on the lines of the intelligence quotient, then he may do so and the present study will provide him with an invaluable starting-point ; but the authors themselves have accomplished quite a different task.

Thus the methodological criticism may be in large measure discounted, and we can accept gratefully this richly detailed natural history of how our awareness of space grows from simple juxtaposition to the manipulation of perspectives and the arguments of geometry. A central theme of the whole account is the important part played in space perception by our own activities. We have inherited from John Locke and the empiricists a view of perception in which the outside world, as it were, imposed itself upon a passive organism. Almost all recent research has shown the untenability of this view, and the present study may perhaps serve to inaugurate a new and quite different approach.

To someone who has at one time wrestled with the original French text, the present translation seems to have been excellently carried out, and any difficulties that the reader may encounter derive from the complexity of the original and not from any defect in the expression.

NEW TECHNIQUES AND APPLICATIONS IN MOLECULAR SPECTROSCOPY

Molecular Spectroscopy

Edited by George Sell. (Report of a Conference organized by the Spectroscopic Panel of the Hydrocarbon Research Group of the Institute of Petroleum, and held in London, 28–29 October 1954.) Pp. viii+234. (London : Institute of Petroleum, 1955.) 42*s*. net.

IT is not so very long ago that self-respecting spectroscopists frowned upon anything more complex than a diatomic molecule. However, the rapid development of the petrochemicals industry has given a great fillip to applied spectroscopy, which has become much more 'broad-minded' with regard to the size of molecules and the complexity of their mixtures that its adepts take in their stride.

Perhaps one of the first of the spectroscopists of the 'old school' who sensed the power of spectroscopic methods as a tool for developing industrial processes was Victor Henri, and indeed nowadays ultra-violet and infra-red methods are necessary tools of the petroleum industry and of many other branches of the chemical industry. To this the present volume bears witness. Yet beyond this it also sheds light on techniques which still have to prove their value for the field of hydrocarbons.

This book is a collection of nineteen papers which were read by invitation at a conference which the Spectroscopic Panel of the Hydrocarbon Research Group of the Institute of Petroleum held in London in 1954. The object of the conference was to bring together people for a discussion of newer techniques. In this endeavour, and in a laudable spirit of being non-parochial, the Panel succeeded in attracting contributions from workers in Britain and overseas. The papers are written by people with widely different interests and touch upon very different aspects of applied spectroscopy. It is only natural, therefore, that they vary considerably in length, depth and breadth.

It is interesting to learn that about two thousand infra-red spectrometers are in use to-day, that cæsium iodide prisms can be made from synthetic crystals to allow measurements to 54μ, and of the possibilities opened up by additively coloured alkali halide crystals as infra-red transmission filters. There is information on gratings for use in the 2–15μ region with line spacings varying from 15,000 to 2,400 lines/inch, on the pressed-disk technique for obtaining spectra of solid materials, on infra-red reflexion spectra from small crystals, on Raman spectrometry, and on infra-red emission from gases excited by a radio-frequency discharge. Gases can be heated to temperatures in excess of 5,000° C. in fewer than ten molecular collisions by the application of shock-waves. For analytical purposes, on the other hand, low-temperature work may become useful where mixtures solidify to transparent disordered glasses. What the analyst is looking forward to very much is to be able to transfer data from one instrument to another ; that is, to assess true intensities from the measured spectra. He derives immediate benefit from a classification of the characteristic vibration frequencies of substituted benzenes. The amount and position of deuterium in mono-deutero-aromatics in the presence of their parent compounds can be determined by infra-red spectrometry. Oxidation plays a great part in the quality and shelf-life of many hydrocarbon products, and infra-red spectrophotometry can be beneficially employed as a yardstick for the degree of oxidation.

Both Raman and ultra-violet spectrometry have their places in type analysis, and there is an interesting account of the determination of aromatic hydrocarbons in lubricating-oil fractions by work in the region of 1900 A. The future will show the part which the flash-photolysis technique and nuclear magnetic-resonance spectra can play in the field of hydrocarbons. There can be little doubt that fluorescence techniques are in the ascendancy. An article of about two thousand words, on the use of fluorescence for industrial analysis and examination, is a masterpiece of concise presentation. The book contains a record of the discussion to each paper, and a discussion on punched cards and the presentation of spectral data forms its concluding chapter.

Workers in the petroleum industry owe a debt of gratitude to the Institute of Petroleum for making available for reference purposes this fountain of information.

R. SCHNURMANN

Electromagnetically Enriched Isotopes and Mass Spectrometry

Edited by M. L. Smith. (Proceedings of the Conference held in the Cockcroft Hall, Harwell, 13–16 September 1955. Sponsored by the Atomic Energy Research Establishment, Harwell.) Pp. xvi+272. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1956.) 45*s*.

THE appearance of this collection of papers on enriched isotopes will be welcomed by all who are interested in this field. These papers are concerned both with the technique of electromagnetic enrichment and with the applications of the enriched isotopes. Since much of the material either has not been published before or is contained in reports of limited circulation, its collection within one volume is an important contribution to the literature of the subject.

More than half the thirty papers are concerned with problems of design in the separator itself. Since the principal factor which determines whether or not an element can be processed electromagnetically is the availability of suitable ion sources and collectors, several papers are concerned with detailed discussion of their construction and of associated chemical problems. It is interesting to note that it is now possible to process in substantial quantities the stable isotopes of nearly all the elements. Abundance measurements and mass-spectrometry are surveyed in a number of papers, and interesting contributions are included on the method of dilution analysis and on a new type of mass-spectrometer employing radio-frequency methods. Other survey papers describe typical uses of enriched isotopes and give some indication of their wide field of application. Two papers direct attention to the importance of applying enrichment techniques to radioactive isotopes.

The book is well produced and contains clear diagrams and photographs. The provision of an adequate index and the inclusion of the discussions which followed the papers add greatly to its value.

M. A. Grace

Protoplasmatologia

Handbuch der Protoplasmaforschung. Herausgegeben von L. V. Heilbrunn und F. Weber. Band 2: Cytoplasma. *A*: Morphologie. 2: Die Submikroskopische Struktur des Cytoplasmas. Von A. Frey-Wyssling. Pp. iv+244. (Wien: Springer-Verlag, 1955.) 72*s*.

DURING the past five years the electron microscope has become the main tool for investigating cellular fine structure. This change in technique is reflected in the much greater space given in this book to electron microscope results than in the earlier work by Prof. A. Frey-Wyssling on submicroscopic morphology. The section on electron microscopy, which takes up the first half of the book, will be most useful to cell biologists. It brings together, for the first time, observations on cell structure which have been scattered through a large number of journals and discusses them in terms of both cell function and molecular morphology. There is an interesting section on the structure of the ground cytoplasm in which Prof. Frey-Wyssling points out the dangers of artefacts and illustrates them with some striking photographs of reticular structure in gelatin and Liesegang rings after osmium fixation. There are a number of good reproductions of electron micrographs, but one could wish for more.

The second half of the book is concerned with those aspects of chemistry, cell physiology and biophysics which are relevant to cellular fine structure. Perhaps the best section is that which deals with the structure of proteins and nucleic acids and describes the recent work of the X-ray crystallographers in this field.

J. M. Mitchison

Physical Chemistry

By Prof. Walter J. Moore. Second edition. Pp. xii+633. (London and New York: Longmans, Green and Co., Ltd., 1956.) 30*s*. net.

PROF. W. J. MOORE uses the thermodynamical approach to physical chemistry, and his readers need a knowledge of advanced mathematics and the ability to apply them. The first edition (1950) was reviewed and commended in these columns (see *Nature*, **168**, 577; 1951). In this, the second American, but first English, edition the author, in bringing the work up to date, has accepted friendly criticism and made numerous small improvements.

The chapters dealing with nuclear chemistry and electrochemistry, and that on the structure of molecules, have all been enlarged. Prof. Moore has extended the scope of the section on photochemistry, has removed it from Chapter 17, on kinetic energy, and has made it into a new chapter on photochemistry and radiochemistry. To the curtailed Chapter 17 he has added two new sections dealing respectively with reactions in flow systems and with the mechanisms of ionic reactions. The lists of articles and books recommended for further reading have been overhauled, brought up to date and extended. Many of the newly listed articles are from the *Journal of Chemical Education* or from the Chemical Society's *Quarterly Reviews*.

The work is recommended to those studying physical chemistry at university level who have the necessary mathematical equipment.

G. F.

Animal Breeding

By Dr. A. L. Hagedoorn. (Agricultural and Horticultural Science Series.) Fifth edition. Pp. xix+364+21 plates. (London: Crosby Lockwood and Son, Ltd., 1954.) 18*s*. net.

PROBABLY no other book has done more than this one to stimulate practical livestock breeders and students of animal husbandry to take an acute interest in genetical principles and ideas. It is fitting that in this fifth edition, with its revisions and additions made by Dr. A. L. Hagedoorn before his death, there should be a memoir of the author by Dr. John Hammond which notes his outspoken critical approach to practical problems and controversies. For his provocative decrial of "fancy points" and show-ring standards, his robust insistence on progeny testing, and his advocacy of the nucleus system of breeding are further emphasized here.

Hagedoorn's own interests in, and practical contacts with, the breeding of large and small animals ranged widely and have once more been freely used for illustrating his main themes and provide the reader with a wealth of observations. Yet the tendency—perhaps need for his purpose—to over-simplify his interpretations of the underlying principles and his advice on breeding problems and procedures remains; while the book can certainly be recommended to be read, it still cannot be accepted without reserve as the full and authoritative word on this aspect of animal production.

J. E. Nichols

CHEMICALLY INDUCED NEOPLASMS IN FUNGI

By Prof. P. T. THOMAS, Dr. H. J. EVANS* and D. T. HUGHES
Department of Agricultural Botany, University College of Wales, Aberystwyth

A NEOPLASM may be defined as a new growth which differs characteristically from that which occurs during normal cell reproduction and differentiation[1]. The benign and malignant neoplasms of animals have naturally, owing to their great importance, been subjected to the most intensive investigations. Unfortunately, animal material is not always favourable for fundamental studies into the factors which determine the origin of these abnormal growths. For this reason attempts have been made to use other organisms, and much useful information has been obtained from the study of tumorous malformations in higher plants[2–7].

From observations and experimental work which we have carried out on a number of fungi we now wish to indicate how this group of organisms may well be particularly favourable for elucidating certain aspects of the problem of cancerous neoplasms in animals. Fungi, unlike higher plants, contain no chlorophyll, and being heterotrophic are, like animals, dependent on nutrients synthesized by other organisms. Many of their metabolic products, for example, glycogen instead of starch, are also essentially similar to those of animals. Indeed, the whole physiology of fungi has so much in common with animals that biochemists have for a long time been using them as physiological models to study "under better controlled conditions, general biochemical reactions of animal tissues"[8].

The degree of control which can be achieved is of major importance, since it includes not only better control of environmental conditions but also of the genetical constitution of the experimental organism.

Interest in this direction was first stimulated by the work of Haddow, who compared the formation of secondary colonies in senescent bacterial cultures with the emergence of a malignant variant in the cells of ageing animal tissues[9]. Later Bausch[10] produced new forms of the yeast *Saccharomyces cerevisiae* by the action of well-known carcinogenic hydrocarbons and also by camphor, which is not known to be carcinogenic in animals. The yeast cells produced were vigorous giant-celled forms and, without cytological confirmation, it was concluded that the effect was due to polyploidy.

From a cytological study of the action of camphor on the asexual yeast *Torulopsis utilis*, Thomas concluded that the significant change in the production of vigorous giant-celled forms occurred in the cytoplasm[11,12]. Multinucleate cells were sometimes produced (Fig. 1); but these were unstable and there was evidence of a 'somatic reduction' to a stable mutant form with a normal nuclear complement and a changed cytoplasm.

From the following considerations it was concluded that there was a close analogy between the action of camphor on yeast and that of carcinogenic agents on animal cells: (1) marked increase in the concentration of nucleic acids, particularly of ribonucleic acid in the cytoplasm and nucleolus; (2) increase in the rate of cell reproduction, that is, reduction in generation time; (3) inhibition of growth during initial stages of treatment by the chemicals; (4) the chemical agents are effective only after a relatively long period of treatment. In yeast, which normally produces a new cell generation every hour or so, the mutant cells appear only after treatment for 2–3 days.

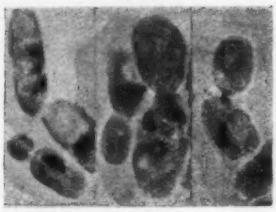

Fig. 1

The type of change which occurs in yeast is essentially in agreement with the view that carcinogenesis involves an optimum inhibition of normal cell growth followed by an adaptation which allows the cells to continue growth[13]. Observations indicate that the chemical agent has a mitostatic effect on the yeast cell nucleus, but at the same time allows cytoplasmic activity to proceed to a new and apparently stable equilibrium.

Neoplasms are more easily recognized when the cells are organized into a tissue or into a pseudotissue as in the fructifications of the larger fungi. Fig. 2*a* illustrates a striking growth malformation produced in the cultivated mushroom *Agaricus campestris* fr. va. *bisporus*, where it has outgrown the normal pileus by at least five times. This tumorous growth is believed to have been induced by the accidental introduction of tarry fumes into a commercial mushroom house. The grower at Aberystwyth was forced to supplement the electrical heating of one of the houses by burning a mixture of coke and coal in open braziers. Between 20 and 30 per cent of the fructifications in the affected house were abnormal; but no such abnormalities were found in another, but smaller, house in which heating by electricity was adequate.

Reference to the literature showed that rather similar but less-pronounced abnormalities had been recorded for the first time in 1930 by Lambert[14]. He proposed the term 'rose-comb disease' and directed attention to its prevalence during 1930 in New York, Pennsylvania, Ohio and Missouri. From his general observations on these abnormalities he wrote as follows: "The agencies that seem most likely to be the cause of the tumours are the coal oil fumes or the fumes or oxidation products of materials containing mineral oil". Atkins, a prominent mushroom grower in Great Britain, also states that mineral oils and coal tar creosote fumes are important agents[15].

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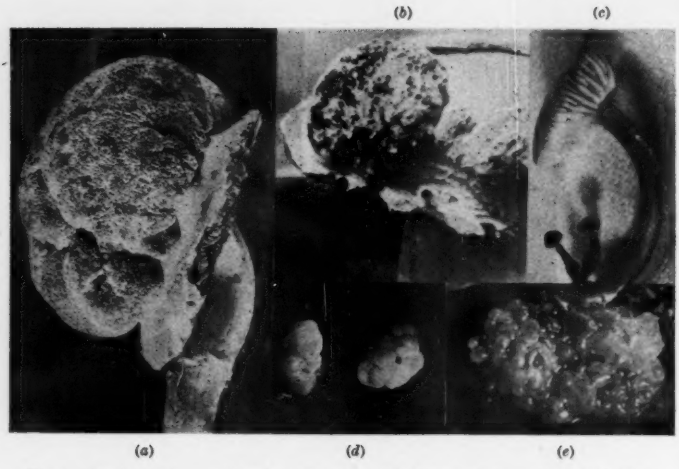

Fig. 2. *Agaric* neoplasms: *Agaricus campestris* with tumorous outgrowths of the pileus (*a*) produced in a commercial crop of mushrooms, and (*b*) induced experimentally by diesel oil vapour treatment. *Collybia velutipes* (*c*) normal fructifications after olive oil treatment. *Collybia* tumours produced after an equivalent treatment with diesel oil, (*d*) at 4 weeks, and (*e*) 8 weeks after initial treatment

One of us (H. J. E.) has carried out experiments designed to study the effects of a number of substances, under controlled conditions, on a commercial strain of the cultivated mushroom. The mushrooms were grown in 9-in. pots on a standard compost and maintained at constant temperature and humidity. Some additional experiments were conducted on mycelium grown in agar culture. A number of pure carcinogenic hydrocarbons were used; but although they had some effect on the growth of mycelium in culture they did not produce the characteristic tumorous malformations when applied to mushroom fructifications. Failure to produce any effect with these hydrocarbons may have been entirely due to technical difficulties involving, in particular, the use of solvents which were toxic to the fungus.

However, volatile mineral oils and coal-tar products could be used directly, and the amount of vapour applied was controlled. With some of these substances tumorous malformations of the type shown in Fig. 2*b* were repeatedly induced. The most striking results were obtained either by treatment with a proprietary substance containing tar acids, or with diesel oil. The latter was by far the most effective agent. Thus, in one series of experiments with diesel oil vapour, tumours were produced on 80 per cent of the mushroom fructifications, after periods of treatment ranging from three to eight days[16]. The maximum amount of tumour production was obtained after a sustained treatment with the vapour at a concentration which retarded development, but was not unduly toxic.

Tumours first appeared as protruberances of the pileus, as early as the young pin-head stage, or later when near maturity. They continued to grow even after the pileus had fully developed. Several distinct tumours could develop on a single pileus; but they often coalesced to form one large deeply lobed tumour. Sometimes, the outer tissues of a tumour differentiated into a spore-producing hymenium resembling that found in the Polyporaceae. (*cf.* Fig. 2*a* and 2*b*.)

Recently, another agaric fungus, *Collybia velutipes*, has shown certain advantages over the cultivated mushroom for experimental purposes. It is smaller in size and can be grown in large quantities in 250 c.c. flasks on a malt–agar medium. It is also found to be particularly sensitive to diesel oil, both in vapour and in liquid form. Treatment was given at the 'pin-head' stage for 14 days, after which the young tumours could be recognized (Fig. 2*d*). Further growth has been observed after up to eight weeks while still under the influence of diesel oil (Fig. 2*e*). Typically, these neoplasms have cerebiform convolutions and there is no differentiation of gill tissue. Fig. 2*c* shows normal development after an equivalent treatment with olive oil. If treatment by diesel oil is delayed until differentiation of the pileus has commenced, fruit bodies the edges of which curl up into tumorous over-growths are produced.

Cytological investigations, so far, have been largely confined to the cultivated mushroom, where comparisons between cell behaviour in normal and tumour tissue have been made[17]. Normal tissue, at the pin-head stage, is composed of closely packed, multinucleate, non-vacuolated cells, each containing an average of six to seven nuclei. Few nuclear divisions occur after the fructification has attained a diameter of about 10 mm. and further development is associated with vacuolation and increase in cell size.

Unlike the surrounding normal tissue, however, the tumours are composed of two kinds of cells, both of which contain actively dividing nuclei (Fig. 3): (i) small, non-vacuolated, multinucleate cells, with markedly basophilic cytoplasm (T_1 cells); (ii) larger vacuolated, multinucleate cells, showing less basophily of the cytoplasm (T_2 cells). In addition, intergrades between these two cell types are found.

The change from a normal to a tumorous condition involves the transformation of normally inactive pileal cells (N_1), with a comparatively low ribonucleic acid turn-over, into actively dividing basophilic T_1 cells. The T_1 cells reproduce their own type and also give rise to vacuolated, less actively dividing T_2 cells. Normal pileal tissue has an average of

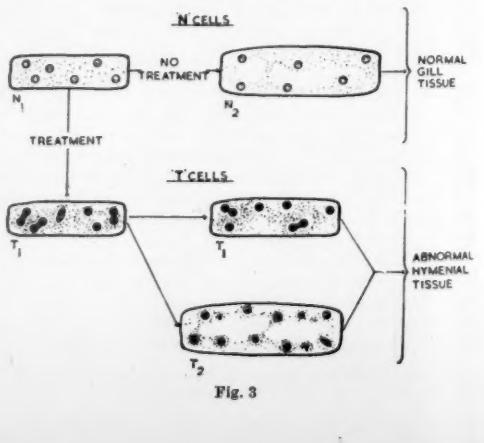

Fig. 3

6·44 ± 0·08 nuclei per cell, whereas in the mature tumour where there is a preponderance of T_2 cells, the average number of nuclei per cell is 10·1 ± 0·36.

In addition to the increased basophily of the cytoplasm and mitotic activity of the nuclei in T cells there is hyperactivity of the nucleolus and heterochromatin. Tumour cells also show abnormal nuclear activity including endomitosis, multipolar spindles, chromosome aggregation, polyploidy, aneuploidy and micronuclei. These cytological disturbances are all characteristic of cells in animal tumours[18,19].

Our observations on a number of fungi serve to emphasize the desirability of undertaking further work on the nature of the changes that are produced by the action of various chemical agents. While fungal cells are not ideally suited for cytological study, there is little doubt that the comparison with the behaviour of cells in animal neoplasms represents something more than a mere analogy. Preliminary work on grafting neoplastic with normal tissue already indicates a promising field of research. Furthermore, the simplicity of organization of the fungi, together with their suitability for culture on synthetic media, should provide ample encouragement for biochemical studies.

We are very grateful to Prof. A. Haddow, of the Chester Beatty Research Institute, not only for his advice and encouragement, but also for supplying a number of carcinogenic hydrocarbons. Our investigations, which will be described in detail elsewhere, have been made possible by a grant from the British Empire Cancer Campaign, to which we also extend our gratitude.

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EDUCATION AND PRODUCTIVITY IN UNDER-DEVELOPED AREAS

THE main theme this year of Section L (Education) of the British Association was education in the British Colonies, and, following Sir Christopher Cox's provocative presidential address, it fell to two symposia to deal in greater detail with two of the central problems involved. These were the relationship of education to productivity, and the central educational dilemma of quantity or quality. Each was the subject of a separate symposium, and Prof. F. C. Benham, of the Royal Institute of International Affairs, opened the first with a paper on "The Allocation of Resources". He pointed out how poor the British Colonies are, with an average income per head of population of only one-tenth to one-seventh of that in Britain. Like all poor countries, they are faced with a difficult choice when they have to decide whether to spend more money on education and the social services, on one hand, or on measures for economic development, on the other. Considering briefly the case for each, Prof. Benham said that many people would urge that absolute priority be given to education, for they would say that illiterates cannot play their part properly as citizens, that children's talents and personalities need to be developed, and that we need higher education to provide leaders in society and government. But in spite of this, education is only one of the claimants among the social services; there are many others, and health and housing, for example, can also make out a very strong case.

On the other hand, the arguments for giving priority to economic development are hard to resist, for unless measures are taken to raise progressively future levels of output and income, there is no escape from a low standard of living. Referring to Lord Beveridge's point that "expenditure on education is the communal investment which in the end will bring the best return", Prof. Benham emphasized that it would be wrong to compare Britain with the Colonies in this respect, for Britain, with a population of fifty million, has a public revenue of more than ten times that of the Colonies. The latter, with a population of eighty million, have an annual income of only £50 million. Moreover, the proportion of children under fifteen years of age in Britain is only 20 per cent, whereas in the Colonies it is 40 per cent.

When a Colonial government considers how best it can use its limited resources to yield the best return, there are likely to be quite a number of projects which will give a greater and a quicker return than education. Considering the matter solely from the point of view of its yield as an investment, education might well have to take a back seat. The case for it only becomes strong when it is considered on its own merits, not as an investment but as a training for life and livelihood and as a means of character-building and raising mental stature. Even so, the Colonies are a long way from their goal, for there are three times as many children in the Colonies as in Britain, and yet only one in three receives any kind of schooling. In the educational field itself, there appear to Prof. Benham to be four outstanding priorities: an adequate flow of leaders at the university-level; teacher-training adequate both in numbers and quality; certain types of technical and vocational education; and, in some Colonies, an agricultural extension service.

Turning to the problem of finance, Prof. Benham thought there were a number of possibilities which might be considered. First, a higher proportion of public expenditure could be devoted to education; secondly, more money might be raised by taxation; thirdly, public loans for education might be raised; fourthly, more external aid might be sought; fifthly, more responsibility might be placed on local author-

ities; sixthly, certain measures could be taken to keep down costs. After briefly considering all these possibilities, however, he did not think he could draw hopeful conclusions from any of them. In spite of all efforts, the root of the difficulty lies in the poverty of Colonial people, and this being so, he thought the only real and permanent solution is to raise their real income by speeding up their economic development.

One of Prof. Benham's priorities was then taken up by Mr. J. C. Jones, director of education of the Regent Street Polytechnic, London, who dealt with the question of "Right Perspectives in Technical Education". Mr. Jones briefly outlined the facilities which already exist for technical education at its higher levels in the Colonies, and expressed it as his personal conviction that a good, general education is essential as a background at whatever level technological education is to be undertaken. This is of even greater importance in the Colonies than in Britain, principally because of two factors—the lack there of a mechanistic background, and the stigma which attaches to manual work. A basic solution to the problems raised by these factors is a greater introduction and emphasis upon educational handicrafts at an early age in the primary school and their continuance into all forms of secondary education. Mr. Jones then went on to describe the facilities which exist in many territories for other than higher technical education and declared that, because of the existence already in most Colonies of a nucleus of technical training facilities, he sees the possibility of a simultaneous development in technical education of both long-term and short-term policies. The former must be directed to a universal system of general education in which some provision is made for pre-vocational training at a relatively early age. The second stage must be the creation of alternative forms of secondary education providing for academic and technical streams. Industry, also, must play its part by the general introduction of apprenticeship schemes wherever conditions permit. Short-term planning, he thought, must be concerned to meet a developing situation in which the increasing demands of industry have to be set against a decreasing expatriate staff. In conclusion, Mr. Jones summarized his beliefs by saying, first, that the system of technical education as applied to under-developed areas can only succeed in so far as it is organically linked to, and continues the work of, the system of general education; secondly, that a system of technical education so applied must relate its work to the whole range of industrial need and not merely to its higher levels; thirdly, that development in technical education must always represent a compromise between long- and short-term policies, one logically conceived in the light of foreseeable economic expansion, and the other concerned primarily to meet the current need. He thought we had good reason to be proud of our past record in effecting the economic, as well as the political, independence of the Colonies.

For many years there has been criticism of the effects of Western schooling in rural, under-developed areas overseas. It has been called bookish and literary and is said to produce a dislike for agriculture, a flight from the land, a distaste for manual labour and a desire to secure black-coated employment. These and other criticisms of Western schooling were discussed by Mr. P. C. C. Evans, of the University of London Institute of Education, in a paper entitled "Western Schooling and Rural Productivity". He attempted to show that, on the whole, these charges against Western schooling are ill-founded, and that it is the humanistic spirit inherent in Western civilization which creates dissatisfaction with the low standard of living associated with the land in the Colonies. This dissatisfaction is not altogether a bad thing, for it leads to new patterns of economic endeavour which in the end will lead to increased productivity. Mr. Evans pointed out how in the past the power of the school to change society in the tropics, whether for better or for worse, has been greatly exaggerated, and that this has brought much criticism upon it for effects which are, in reality, due to the whole Western contact. Even so, in order that the standard of living may be raised, and the basic values of Western civilization find fuller expression, it is necessary that schooling at all levels should be permeated with a rural idiom, which will direct pupils' endeavours, by means of a pragmatic, problem-solving approach, to deal with the urgent problems of community living.

Perhaps the most arresting, and certainly one of the most interesting, talks of the whole symposium was that given by Mr. R. K. A. Gardiner, recently director of the Gold Coast Department of Community Development, who spoke on "Fundamental Education and Economic Development". Perhaps unconsciously, all the speakers so far had appeared to give what could have been described as a European point of view; but Mr. Gardiner, an African, showed how, in some respects, our perspectives need adjustment. He referred, for example, to Prof. Benham's insistence on the scarcity of material resources, and then pointed out that the Colonies have one rich resource which is rarely given full credit—the people themselves. Their free labour, self-sacrifice and goodwill are assets of great importance in promoting improved living, and the means of tapping these is through community development. How successful the Gold Coast Department of Community Development had been in this Mr. Gardiner illustrated in a number of striking examples. Five hundred cacao-tree sprayers had been bought by the Agricultural Department to fight swollen-shoot disease; but cocoa-farmers would not buy them. The Department anticipated that it would take about five years to sell them all. It enlisted the help of the Community Development Department, and after a short campaign by the latter all the sprayers were sold in a couple of months. Again, an important road estimated to cost a very considerable sum to build had already been half-built, with the help of voluntary labour and savings, for only £100,000. But Mr. Gardiner reminded his audience that in dealing with people it must be remembered that they are not malleable material, but human beings who matter. His eloquence and simple sincerity made a fitting conclusion to a most interesting symposium.

The task of the next symposium was to discuss "The Central Educational Dilemma in Underdeveloped Territories: Quality or Quantity", and Mr. E. W. Woodhead, chief education officer for Kent, opened it with a paper entitled "The Problem of Priorities". He pointed out how the administrator in such countries will be unlikely to have at his disposal adequate resources in money, staff or materials. Again, people on the verge of self-government see priorities differently from those a long way from it. As self-government approaches, so a desire for Utopia within a limited period grows up. A new

sense of urgency arises, marked by a new relationship between government and people and often an unwillingness to recognize stubborn facts of inadequate resources, insufficiently trained staff and limited experience. Unless the administrator recognizes and accepts these new attitudes, it may not be possible to moderate harmful effects and gradually to establish worth-while standards. The approach to self-government is reflected also in the changing aims and emphasis in education, which now comes to be regarded as one of the keys to self-government and to a sense of equality with Western powers. Such aims must for a time dominate the educational scene, though other aims must not, in the process, be forgotten. For no country, said Mr. Woodhead, can reach nationhood without the development of a public morality, co-operative attitudes in its citizens and a willingness to accept responsibility. These personal aims need to be retained alongside the demand for greater knowledge and improved skills.

The growth of an education service in the Colonies, continued Mr. Woodhead, seems to pass through a number of fairly clearly defined stages. First, it provides an escape for the few from reality and the hardness of life. Then comes a mass demand for education, associated with the introduction of cash-crops or the growth of industry. This is a stage dangerous for standards, and needs to be passed through as quickly as possible. Then comes the third stage, one dominated by a political emphasis and a demand for universal primary education and the development of secondary schools. For each of these stages there must clearly be different priorities in the educationist's mind. The administrator's problem now is to ensure as wise action as possible at each stage, though, in any case, he will find his plans affected by many factors beyond his control.

In the development plans of most Colonies the goal is universal primary education with such secondary and further education as will meet urgent needs. Yet the problem is always one of how to meet new educational demands with limited resources. There are few features of life in these countries which so manifestly have such political priority as the education service. This political demand often outruns the wise use of resources and the establishment of good educational standards. The administrator is pressed, on one hand, to go ahead by the political situation, and, on the other, he is held back by economic considerations which are sometimes ignored by newly independent peoples. The chief challenge comes from such places as the Gold Coast, Nigeria and Malaya, where the pressure of the demand for education is in danger of submerging for a time the quality of the work undertaken.

Mr. Woodhead then reviewed briefly what seemed to him important priorities at each educational level. Something could be done to safeguard priorities in primary education by avoiding a complete dispersal of trained staff and by retaining a few good schools to serve as the guardians of standards. At the secondary school stage he stressed the need for alternative provision to grammar school education. Here again the maintenance of good standards lies in the hands of a few schools. These good standards, he thought, should be high on the list of priorities, especially since secondary education must for a long time be selective rather than universally available. The highest priority of all he would accord to teacher-training, for the preparation of really good teachers is the spearhead of educational progress. In dealing with educational administration and personnel, Mr. Woodhead stressed that two important priorities affecting standards and quality are the administrative framework and the adequacy and suitability of its personnel. In the former there is an important part for the voluntary agencies, private schools and the development of local authorities. Inspection and supervision also must be improved if minimum standards are to be maintained.

In conclusion, Mr. Woodhead indicated what are to him a number of keys to quality. The responsibility for both quality and quantity must rest with the government of the territory. Care must be taken when building on inadequate foundations in primary and secondary schools in preparation for sixth forms, universities and teacher-training. The key points for the preservation of quality of work and development are the grammar school and the training college. Where choice exists, emphasis must always be put on persons of quality, whether officer, teacher or child. He thought that a few really good schools and institutions for further education should be developed in order that these might leaven the whole educational service. Every effort should be made to recruit local officers with suitable training, though expatriates should be retained where necessary in order that the best experience of the past might be available in new situations.

The problem of building secondary education on insecure foundations under pressure from a quickly developing higher educational system was the theme of a talk by Sir James Robertson, rector of Aberdeen Grammar School, when he spoke on "The Demand for Higher Education". The strain on secondary education, said Sir James, comes chiefly from the fact that it is sandwiched between primary education, on one hand, and the universities on the other. He referred to the limiting factors mentioned by earlier speakers in connexion with under-developed countries —the smallness of the resources available and the stubbornness of local educational demands. At the moment the latter can conceive of secondary education only in terms of the British grammar school, and there is a tremendous demand for formal British education because it leads to enhanced personal status and advancement. But the provision for secondary education is very small. In the Gold Coast, for example, only 2 per cent of the school population is in secondary schools, and this is a country well advanced towards self-determination. Sir James sees a number of obstacles in the way of efficient secondary education—obstacles such as insufficient preparation at the primary stage, the immense gap between local conditions and Western civilization, and the great difficulty of crossing from vernacular literacy to a facility in the English language. All these are weaknesses of the primary school; but they reappear in acute form in the secondary school and lead to a situation where pupils know words but not realities, where speech becomes vague and abstract, and where an obsession develops for examination results.

In addition to these educational problems, there are the forces of nationalism and independence, which force the pace by demanding more training college staff and quicker replacement of Europeans by local people in the education service, and which lead to compulsive demands from university and technical colleges for more students. The British have written one of the great chapters in their Colonial story in setting up the new university

colleges; but in some ways they have to pay the price, for national pride and aspirations are not satisfied with the meagre provision for higher education that is warranted in view of the poor schools. These latter could do with a period of patient quiet to develop; but, as it is, good teachers who could not be spared had been diverted to sixth-form work. In the end, this may prove a good thing, for sometimes it pays to be stretched educationally, and the schools will be compensated by receiving back a stream of good teachers. But for the period ahead in the development of secondary education, Sir James said that two things are necessary: schools must keep up standards in their lower forms and improve their English, and, if a rapid expansion of secondary education comes, good staffs must not be dispersed. A few good schools must be kept going while standards are being raised elsewhere.

Miss F. Gwilliam, assistant educational adviser to the Secretary of State for the Colonies, then spoke on "The Challenge to Teacher-Training". She asked three questions: Who are the teachers, what standards are they trying to preserve, and how are they meeting the challenge? The teachers themselves, said Miss Gwilliam, have greatly varying backgrounds and qualifications, and often they were of many nationalities. There are Austrian nuns, American missionaries, teachers from Britain who have gone out through the Overseas Appointments Bureau, the personnel of the Colonial Education Service and the local teachers themselves. All these, said Miss Gwilliam, are the teachers. The standards they are seeking to preserve, she thought, are of four sorts—academic, personal, professional and civic standards—and to maintain and improve them constitutes the challenge to teacher-training. In the different territories of the British Colonies this challenge is being met in a number of ways: local training colleges are being built in increasing numbers, scholarship funds are being provided to send students to Britain for training, and 'on-the-spot' vacation courses are being run for practising teachers. The teachers themselves are taking full advantage of these facilities, and in Cyprus, for example, 80 per cent of primary school teachers take part in unpaid, voluntary vacation courses. The in-service training schemes of the Gold Coast and the Malayan training colleges in Britain are other outstanding examples of the way in which the challenge is being met. Behind all these efforts, said Miss Gwilliam, lies the educational resources of Britain in inspiration, advice and help.

The symposium was brought to an end by Mr. Philip Sherlock, vice-principal of the University College of the West Indies, who spoke on "National Aspirations". Speaking with great eloquence and clarity, Mr. Sherlock, himself a West Indian, reminded his audience that Britain had long had a well-developed sense of nationhood. This the West Indies lacks. The great task there is to bring together a great variety of strains and races and to build from them a common nation. They have to fashion a new society, unlike the Gold Coast and Nigeria, who are seeking to rebuild an old one. It is in this task of nation-building that the contribution of the West Indies to the world and human understanding lies, for to do this successfully means a great emphasis on human relationships, and perhaps in this the West Indies may have something to offer others.

Mr. Sherlock paid great tribute to Britain for its help and foresight in setting up the new University College of the West Indies, for this, he said, is basic to the whole task they have in hand. The West Indies and the United Kingdom now stand as partners in the great enterprise of finding new patterns of social development. But this, he emphasized, is not a one-way process. Both sides will profit. The West Indies wants from Britain advice on an expanding secondary school system, on teacher-training, library services and other matters, and in return Britain might profit from the lessons learnt in what is a tremendous, dynamic move forward by the peoples of the Caribbean.

After each symposium there was a discussion in which the audience participated. Contributions were made by county education officers, professors of education, training college staff and local teachers, all of whom expressed the hope that there would be, in the future, even greater collaboration between Britain and the oversea territories in the task of promoting the latter's educational advancement.

P. C. C. Evans

PHYSIOLOGY IN THE POLAR REGIONS

During the meeting at Sheffield of the British Association, Section I (Physiology) arranged a session on September 4 on "Polar Physiology".

The degree of physiological adaptation to cold by man is still an unsettled problem. Although there is convincing evidence that laboratory animals can be so acclimatized that they will survive at temperatures which are lethal to control animals, chronic physiological changes in man as a result of exposure to cold have not been clearly established.

Many studies have been made in climatic chambers, in which men can stay for relatively prolonged periods in a controlled environment. Changes have been looked for in the rate of body cooling, alterations of skin temperature, changes in metabolic rate, time of onset of shivering, alteration in the peripheral blood flow and shifts of the blood volume. There has been a number of reports indicating some change in one or more of these parameters as a result of repeated exposure; but there have also been many negative reports. One of the practical difficulties of experiments in climatic chambers is to persuade subjects to stay in such chambers for long periods. There are indications that some significant physiological changes develop slowly over a period of many weeks or months. It is for this reason that observations have been sought on polar explorers, who spend one to two years at high latitudes. Many of the members of polar expeditions are trained scientists and can make accurate and systematic observations on themselves. Detailed investigations of the subjects can also be made before and after prolonged sojourn in the polar regions, in laboratories in the country of origin.

Apart from low temperatures, another environmental characteristic of polar regions is of interest to

physiologists. In high latitudes, the cycle of light and darkness varies greatly during the year, with approximately three months winter darkness and three months summer daylight. There are many biological diurnal rhythms, and it is of considerable interest to know how these rhythms in man may be affected by alteration in the pattern of day and night.

Dr. Harold Lewis, who accompanied the British North Greenland Expedition of 1952–54 as physiologist, showed a film illustrating some of the physiological problems encountered, and which demonstrated very vividly the effects of light and darkness. He also read a paper entitled "Sleep and Wakefulness Patterns in Men on a Polar Expedition". Records were kept by the members of the expedition of the hours spent in sleep each day. During the autumn and the spring, the patterns of sleep resembled those commonly observed in temperate countries. The majority went to bed between 10 p.m. and midnight and got up some eight hours later. When the sun disappeared for the long winter night, the pattern became increasingly disrupted, and the different individuals were going to bed or getting up at all hours. There was never a time when someone was not in bed or someone out of bed. Sleep was no longer restricted to the hours between 10 p.m. and 8 a.m. The intervals between periods of sleep varied greatly and so did the length of each period of sleep. A similar disruption of sleep was observed during the months of continuous daylight. These changes were observed in both years during which the expedition was in North Greenland. There did not appear to be any tendency for adaptation to the day–night pattern.

There are a number of interesting questions on sleep behaviour which can be asked as a result of these observations. Particularly during the winter months when opportunities for field-work were severely restricted, there was relatively little to do. There was no social compulsion to get out of bed at any particular hour, and opportunities for sleep were to all intents unlimited. The situation was analogous to that of 'demand' feeding in infants. Where records of the number of hours spent in sleep have been kept, in Britain and in the United States, the average is found to be approximately eight out of the twenty-four. On the North Greenland Expedition the number of hours of sleep averaged 7·9, and there was little difference for any month of the year. So it would appear that eight hours of sleep a day does represent a normal demand. There was no evidence that the incidence of light or darkness affected this average duration of sleep, although there was possibly an increased variation in the number of hours of sleep in twenty-four hours during the winter months.

Dr. Mary Lobban followed with a paper, "Studies on Physiological Diurnal Rhythms in Polar Regions". In the summers of 1953 and 1955, two expeditions went from Cambridge to Spitsbergen to study the effects of prolonged periods of life with abnormal time routines upon physiological diurnal rhythms in man. In Spitsbergen the climatic conditions are such that a very high latitude can be reached with comparative ease in the summer months, and human subjects can be maintained there for considerable periods of time in isolation and under conditions of almost constant daylight and environmental temperature.

In 1953 eight subjects lived for six weeks on a 22-hr. 'day', while in 1955 one group of seven subjects lived on a 21-hr. 'day' and another group of five subjects lived on a 27-hr. 'day' for a similar period. In all three groups, urine samples were collected from the subjects at frequent intervals on experimental recording 'days' and a complete study was made of their diurnal excretory rhythms throughout the experimental period. On these recording 'days', diet, fluid intake and all physical activities were carefully controlled. During the 1955 expedition the diurnal variations in body temperature were also recorded.

From the results obtained on the two expeditions it would seem that rapid adaptation of the urinary rhythm to an abnormal time routine is an uncommon occurrence. In nearly all the subjects on all three time-scales, the intrinsic 24-hr. excretory rhythm persisted to a greater or lesser degree, and in some it was maintained unimpaired for the whole duration of the experiment. Subjects who failed to become adapted to the environmental time routine showed signs of stress, particularly at those times when their excretory rhythms became greatly disorganized. In at least three subjects on the 1955 expedition, the disorganization of their excretory rhythms was peculiarly complex, in that a complete dissociation occurred between the rhythms of the excretion of water and of potassium. Further evidence for the dissociation of physiological rhythms was provided by the body-temperature recordings; in all subjects on both 21-hr. and 27-hr. routines, the body-temperature rhythm appeared to become adapted rapidly and completely to the environmental routine, irrespective of the degree of adaptation manifested by the excretory rhythms.

These experiments provide evidence for the persistence of the intrinsic, 24-hr. rhythm of kidney function in some human subjects; they also indicate that the mechanism which controls the normal diurnal variations in body temperature is not the same as that controlling the excretory rhythm.

Dr. J. P. Masterton, who was the medical officer on the British North Greenland Expedition and collaborated with Dr. Lewis in the physiological work, read a paper on "Nutrition and Energy Expenditure during a Polar Expedition".

There is still a lively controversy on the effects of temperature on food intake and food requirements. Investigations during the Second World War showed that the consumption of food by American soldiers rose as the temperature fell, and there appeared to be an inverse linear relationship between the two. Recent investigations of the diet of Eskimo and other inhabitants of arctic Canada and Alaska show that the calorie intake in cold countries may be little different from that in temperate countries. There have been only a few measurements made of energy expenditure in polar regions, so knowledge of food requirements is largely based on the accumulated experience of different expeditions.

Dr. Masterton measured the food intake of four men during the winter when they were living in the base hut. The daily individual intake was recorded for two periods of one week each, with a month's interval between the two weeks. A diary was kept of the activities of the subjects during these experimental periods, and from this, together with the measured basal metabolic rate, the energy expenditure was computed. There were wide daily variations both of expenditure and intake during this period, the range being 1,990–8,760 Calories consumed, with a mean value of 3,908. Expenditure varied from 2,220 to 5,890 Calories, the average being 3,510.

According to these calculations, the men were in positive food balance, and this finding is supported by the result of the measurements of body-weight,

which showed substantial increases during the winter. Food was not limited at the base hut, and substantial snacks could be prepared by individuals apart from the regular meals.

The same subjects were out sledging for prolonged periods during the spring, and measurements were made of intake and expenditure during ten days. A high-calorie ration was provided; but the possibility of supplementing this was limited. The intake was much more constant, the range of forty observations being 4,000–5,500 Calories, with a mean of 4,800. Expenditure, on the contrary, varied much more, as weather on occasions prevented sledging, and a whole day would have to be spent in the tent; the range was 2,230–7,670 with a mean of 4,950. There was loss of weight during these long sledging journeys, which is consistent with the estimated negative calorie balance.

Although it is not possible on the basis of these results to be dogmatic about the effects of cold on food intake, they form a valuable basis for future work. A mean daily calorie expenditure of nearly 5,000 Calories represents very hard work, and it will be of great interest to have accurate metabolic measurements.

A food intake of 3,900 Calories in the base hut is also high, although not so high as some predictions of the effect of cold might indicate.

Dr. Masterton started his measurements because it was noted that the huskies ate human fæces voraciously in spite of the apparently adequate diet provided for them. It was considered possible that there might be a considerable excretion of fat in the fæces, in view of the high fat content of the diet both at base and while sledging. Analysis of the fæces showed, however, that the fat content was low, so the reason for this dietary habit of the dogs remains unexplained. There are a number of problems concerning the nutrition and energy expenditure of huskies which have not been previously studied. Mr. Julian Taylor described briefly some of the work he had done during the past two years while he was a member of the Falkland Islands Dependencies Survey, and specially studied dog physiology. He calculated energy expenditure during sledging by measuring the pull exerted, and recorded body-weight changes together with the food intake. Although the food consumption was high, being of the order of 2,800–3,000 Calories per day, there was considerable loss of weight during long journeys. Mr. Taylor estimated that the energy output was of the order of 4,000 Calories per day. This is a very large figure, as the weight of the dogs was of the order of 90 lb. Examination of the fæces showed that there was relatively poor utilization of the diet. Mr. Taylor emphasized the need for further studies on the physiology of husky dogs, and pointed out that dog teams still play an essential part in polar travel.

Studies on acclimatization to cold were presented by Dr. Paul Massey, who acted as medical officer for the Falkland Islands Dependencies Survey. He used Mackworth's *V* test for measuring changes in local acclimatization to cold in the fingers. By means of this test, the tactile discrimination of the finger is measured before and after the standard exposure to cold, and Dr. Mackworth has shown that there is a diminishing loss of finger numbness during repeated exposure of subjects in a cold chamber. Dr. Massey was able to study members of the Falkland Islands Dependencies Survey on Graham Land, some of whom were newcomers and others who had already spent a year or more in the Antarctic. Initially there was a marked difference between the two groups, those with antarctic experience having a much smaller loss of sensation in the finger after exposure to cold. This difference diminished during the first six weeks in Graham Land, and thereafter there was little difference between the two groups.

These results indicate that there is a fairly rapid local adaptation to cold. However, Dr. Massey believes there is probably a longer-term adaptation, as on several occasions there was mild frostbite of the exposed fingers during the test. These, however, only occurred in the newcomers.

Dr. Allan Rogers, who has been appointed as physiologist and medical officer to the Trans-Antarctic Expedition, 1955–58, described the programme of physiological research which he plans to carry out on the Expedition. He pointed out that this is a unique opportunity for physiological investigations, as the journey itself will probably occupy some four months and involve a considerable degree of exposure to cold. The work to be done on this expedition is a direct continuation of physiological work carried out on the British North Greenland Expedition, and has been planned with the help of the Medical Research Council. It is not possible to carry out elaborate experiments, for the working conditions during the crossing will be difficult, and the physiologist will also act as medical officer and dentist and will have the responsibility of veterinary work for dog teams. No heavy or bulky apparatus can be taken, as food and fuel will occupy almost the whole of the available space during the crossing.

In view of the practical importance and theoretical interest of the effect of cold on food intake and energy expenditure, the main investigation on the fifteen members of the Expedition will be an attempt to make an energy balance. Dr. Rogers will be taking with him an instrument designed by H. S. Wolff—the integrating motor pneumotachograph—for the measurement of oxygen consumption. The advantage of this apparatus is that it can be worn for long periods of time without interfering with the activity of the subject, and it has been so modified that it can be used at low temperatures. It is hoped that the members of the Expedition will be able to keep detailed diaries recording their activities, including hours of sleep, and also of clothing worn. Such diaries have been kept on other expeditions, and although the information so far obtained is not sufficiently systematic, it does indicate that the amount of clothing worn in the cold diminishes with prolonged life at high latitudes. This is certainly suggestive of adaptation to cold.

The experience which has been gained in the past few years by members of the Medical Research Council in developing physiological work on expeditions has shown that there are three important points to be realized: (1) that physiology must be an accepted object of the expedition; this is particularly important, as at this stage systematic observations at frequent intervals are necessary; (2) such observations should be carried out or supervised by a physiologist, or a medical officer with some special training in physiology; (3) only simple observations or experiments should be attempted; these principles were well illustrated in the case of the Trans-Antarctic Expedition, in which physiology is, thanks to the enthusiasm of Dr. V. Fuchs, an accepted object of the Expedition, and an experienced physiologist has been appointed. O. G. Edholm

METAL FATIGUE IN THEORY AND DESIGN

By Dr. A. J. KENNEDY
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An international conference on the fatigue of metals, sponsored by the Institution of Mechanical Engineers, in co-operation with the American Society of Mechanical Engineers, was held in London during September 10–14. Some eighty papers were presented, covering the whole range of interests in fatigue, both academic and technological. Contributions were made by authors from Australia, France, Germany, Japan and the U.S.S.R., as well as from the United States and Great Britain. More than six hundred scientists and engineers attended the meetings, and the discussions on the papers brought in contributors from many more countries. The papers are to be read again in New York at a second conference during November 28–30, and the whole of the proceedings, with the discussions from both centres, is to be published afterwards in a single volume. The enterprise is the most ambitious of its kind yet attempted, and occurs at a significant stage in the development of fatigue theory and machine design.

The conference covered so wide a range of research that no short report could do justice to the detailed information presented. Certain general observations on the subject can, however, be made, prompted and shaped, as it were, by the discussions which took place. These can be very usefully viewed against the background of past development, and suggest the way in which the subject may evolve in the future.

Fatigue in metals, and in solids generally, has been plagued with an inappropriate title and an inaccurate popular press. As a subject it is really quite old. The early observations, being far in advance of understanding of the solid state, gave rise to a terminology, and even a philosophy, which have hampered scientific thinking ever since. Criticisms are repeatedly lavished on the scientists for their failure to communicate ideas and findings in a way which all can understand. This proves a most admirable exercise, but it seems hard that the scientist, who deals with difficult and often esoteric mathematical concepts, should be selected as the plain man's scapegoat, good material though he may be. He might reasonably, at times, ask for a little less plainness at the other end.

In the case of fatigue, however, much of the responsibility for the popular misconceptions rests squarely on the scientific exponents. Intentionally or otherwise, the doubts and dissensions within the subject are popularly interpreted as revealing a general ignorance of its nature, cause and effects. Recent failures in aircraft appeared to give point to this. In fact, there is, in certain directions, a surfeit of information on the subject; test data have been loading down the technical press for years, following the much careful and laborious experiment that has been undertaken in establishing the importance of a variety of practical factors. The general answer to the popular legend that metal fatigue is as prevalent and as little understood as the common cold is supplied by every aircraft, or every engine, which does not fail during its design life. These are the successful products of anti-fatigue methods, for which engineering science should be given every credit. Of course, there is uncertainty about the fundamental nature of fatigue. But the theories of the mechanical properties of metals generally are still very conjectural, and it needs to be remembered that the microscopic mechanics of the solid state have turned out to be far more difficult to understand than its chemistry or its metallurgy, in the structural-compositional sense. Problems involving, essentially, the structures of atoms, and the differences between such structures, supremely difficult though these may be, have gone forward more readily than those involving the forces between atoms in aggregates, whether solid or liquid. It was, of course, in order to deal with these difficulties that the idea of a crystal imperfection, or dislocation, was first introduced. While this idea fitted at once certain observations on the nature of slip in single crystals, it is only during very recent times, indeed during the past ten years, that the theory can be said to have established itself as a fruitful study in its own right. It now has a number of successes to its credit, of various kinds; but these are recent and involve fairly simple systems, such as, for example, pure single crystals under restricted conditions of stress and temperature. It is therefore unreasonable to expect that such an involved problem as the behaviour of complex alloys under complex stresses and conditions should be particularly well understood, or even that some single answer exists.

This latter assumption, that all failures under alternating stresses can be lumped together as the consequence of some unique process called fatigue, needs to be strongly dispelled. Useful mechanical metals have a complicated structure, and are subjected to a complicated thermal and stress treatment. They are made up of regions of differing composition, some of which may in turn possess a form of internal substructure. Each particular type of region, in isolation, may have quite different characteristics of deformation from the others, and the boundaries between such regions are also mechanically very different.

Nor are the internal stresses uniform. On the atomic scale, a number of mechanisms can occur in such aggregates: structural transformations of various types, diffusion, recrystallization, ageing, recovery, slip, polygonization, relative movements of boundaries, and so on. The operation of these mechanisms is frequently markedly directional, that is, a general anisotropy exists. At certain points quite distinctive changes may occur under alternating stresses characterized by an apparent concentration of plastic strain. In some alloys, it is interesting that an actual extrusion of material may occur at the slip band. Ultimately it is possible for small cracks to form at such sites, and some of these will be propagated, possibly to failure.

There are, then, two phases in the development of fatigue. First, the process of crack formation, and secondly that of crack propagation. It can be demonstrated that the crack usually appears at

points of high local slip; but the development of such a crack must obviously depend in some way upon all the other processes taking place. Frequently all these processes are taken collectively to constitute what is termed fatigue. On the basis of present knowledge, this seems unnecessary and misguided. The fact is that a number of processes occur, and the partition of the stress energy between these depends greatly on such factors as stress, frequency and temperature, on the geometry of the system, and indeed on the chance arrangement of the constituents of the structure. It may be that future research will show that no special or singular mechanisms are required to explain crack formation by fatigue, but only the extension of others already recognized and established. At present the question is an open one. In any event, it will be evident from what has been said that, although we still have to explain how cracks may be formed in the slip-bands of crystals under alternating stresses, and to account for the differing nature of the local deformation as compared with uni-directional stressing, a number of possible modes of crack formation may arise in a complex alloy, giving rise to cracks at quite different sites under different conditions. Some discipline in our thinking is here much needed, for the idea of some single basic mechanism is deeply rooted. It is strange that this should be so, for we do not attempt to force the observations in other fields, such as those of brittle fracture, creep and ageing, into a single-mechanism explanation.

Once formed, and depending on the stress pattern and the nature of the material, a crack may be propagated. We might again well ask why this final phase should also automatically be brought together under the same general heading of fatigue. Cracks can be introduced in other ways, by quenching for example, and their propagation need have nothing whatever to do with the fatigue process as we imagine it. Some caution is necessary here, because the propagation is itself obviously dependent on the nature of the material traversed by the cracks, and it may be that the development of what might be termed the genuine fatigue process reduces the overall ductility and hence speeds the crack propagation. It is dangerously easy, then, to label all crack-forming processes, such as those that occur during corrosion, as fatigue, and hence to lose the significance that should be attached to the term.

In general, then, it seems that too much has been brought together under the title of fatigue, and that as a consequence the fundamental problem has become obscured. The problem remains, simply, why a fracture can occur in a pure single crystal (that is, in a regular lattice) under alternating stresses of a value which would not lead to failure if applied uni-directionally. The physicists seem reasonably agreed among themselves that dislocation theory can supply the answer. As it stands, the theory is now capable of demonstrating how vacancies may be generated by moving dislocations, and how these vacancies may bring about the observed increase in the speed of recovery from any residual straining. So far as the formation of an incipient crack is concerned, the collection of vacancies into clusters is taken to be the essential operation, and a mechanism for this has been proposed. No one would quarrel greatly with the general dynamics of the process as set out, and it is only fair that the theory should be allowed to prove its points, where relevant, by drawing on results, established elsewhere, of a rather different character. The theory may, in other words, establish a working model before it is fitted up around the fatigue problem, and this is indeed what has happened.

The engineers, for their part, can scarcely be blamed for being unconvinced by these tactics. Much of the theory they have necessarily to take on trust, and they feel that it is no solution simply to select from the several dislocation and vacancy mechanisms which are theoretically possible the one that best fits the facts. A much more critical experimental approach is required to demonstrate why a certain sequence of events takes place rather than another. To establish this it may be necessary to cast the experimental net much wider, and to bring in other properties, an understanding of which is already more firmly grounded. Electrical properties, particularly under conditions of extreme temperature, may be useful in affording such cross-links and in thus strengthening the whole theoretical structure. Generally, engineering has been little helped in its day-to-day problems by the more fundamental physical research. This is in many ways understandable, once the scale of the difficulties is appreciated. What is much more difficult to justify is the slight statistical treatment which the problem has attracted. Even if causes are difficult to sort out, the effects, whatever they may be, ought to provide plenty of good material for statistical analysis. There has in fact been work on these lines, and very excellent some of it is; but the infiltration of the methods into the design field, and the replacement of outdated design factors, is long overdue.

We have to admit that engineering advance, in the face of such difficulties as that of fatigue, has been gained largely by the application of what might be called the classical principles of design. More and more ingenuity has been required as the operating conditions have increased in severity, and some short relief has been obtained by the development of new high-temperature high-strength alloys. On the whole, the traditional methods of testing, coupled with established principles of stress relief, have enabled technological practice to keep up with the demands made upon it. There are, however, no large factors left in the equations. Even where some distinctive improvement in the properties of metals may be anticipated, it is quite certain that this will be quickly swallowed up by an immediate raising of design specifications. Fatigue, then, will always be with us. Supersonic machines, rockets and high-temperature gas turbines are already a reality, but their performance is below, well below, that required of them in the future. The conditions to which they will most certainly be subjected will not only be severe in themselves, but will also provide a combination of stress and temperature conditions under which fatigue, as a single factor, will be of no interest whatever. The important problem will be the survival of machines as a whole, under the complex working conditions imposed. This means their survival under repeated cycles of thermal shock, fatigue and creep, together with any other processes, such as corrosion, which may arise, the actual history being made up of both regular and random components. Although it is generally agreed that full-scale tests on major assemblies (such as aircraft) are here to stay, despite the cost, it seems worth remembering that in the case of high-speed flight the working conditions may not be reproducible at all in test form.

We are, then, confronted with a situation which differs from the past not merely in the degree of the problems faced, but in their quite revolutionary nature as well. We now have to design for change in machines, knowing that they will change and knowing that they will fail. The material design no longer demands simply knowledge of a set of static factors, but requires information on dynamic processes with statistical characteristics. The traditional methods will certainly go on indefinitely fulfilling their purpose in many fields, and they will improve; but if the materials barrier, as it may be called, is to be broken, a quite new philosophy of design is required. Whatever may develop in the future, it is certain that a mere scaling-up of the test resources, a continued amassing of data on individual properties, and a hand-to-mouth selection of material will be inadequate, however good the basic design may be. At present, not even the faintest framework of a solution exists; but there is a growing awareness of the need for some part of science and engineering to concern itself with the possibilities of quite new methods of design, particularly in the selection of materials. Such studies cannot be made without getting well away from particular problems of detail and seeing the full implications of the changes as they affect the methods of testing, the nature of the test data, the extraction of empirical factors and the use of such factors in actual design. Complex testing, so far as both stress and temperature are concerned, seems likely to replace much of the single-property fixed-conditions testing at present undertaken. The assembly of the data into a suitable usable form is bound to be fraught with great difficulties. But computing and data-processing techniques have transformed similar situations elsewhere, and encourage hopes of some success in this direction as well.

We may sum up somewhat as follows. Fundamental science needs to order its ideas on the processes which occur in metals under alternating stresses, and to be more rigorous in the distinctions drawn between fatigue and other parallel processes. The theories, though superficially sound, are facile and lack the conviction which only critical experiment can give them. The bulk of applied work on fatigue continues very successfully, according to established principles, and one by one the numerous engineering factors are being run through. There is an improved agreement between different centres of research following the better design of test machines and the recognition of differences between them, but there is a real need for an infusion of statistical theory. For the future, engineering design needs to be supplemented (not replaced) by a quite different approach involving new and, at present, unknown methods, in which fatigue takes its place as one of several interacting processes which combine to bring about, inevitably, a failure of the machine.

Conferences on the scale of the one recently held in London involve a prodigious amount of work and planning, both technical and administrative, and something more than a formal acknowledgment to the bodies concerned is required. The quality of the organization does all concerned great credit, and due to their efforts a real and effective contribution has been made to the subject. The final proceedings, when published, will be on a scale quite unlike anything attempted previously, and will surely in time become established as a major work of reference.

OBITUARY

Prof. John Garstang

JOHN GARSTANG was born in 1876 at Blackburn, where his father, Dr. Walter Garstang, was a well-known physician. After leaving Blackburn Grammar School, he went to Jesus College, Oxford, with a mathematical scholarship, and graduated in 1899. While still an undergraduate his interest in archæology had been awakened, and from 1897 for some nine or ten years he undertook research and excavations at various sites of Roman Britain, particularly at Ribchester, Melandra Castle, Richborough and Brough.

His first visit to Egypt was in the winter of 1900, when he excavated at Mahasna and Bet Khallaf for the Egypt Research Account. In the following winter, supported by friends in Liverpool, he excavated on his own account in the same district. By this time he had been introduced to University circles in Liverpool, and in 1902 he was appointed honorary reader in Egyptian archæology in the University of Liverpool. During this and the following years Garstang campaigned tirelessly to stimulate interest in archæology in Liverpool. These were the years when the University was about to obtain its charter and his appeals were not ignored, for an influential group of Liverpool citizens was specially interested in ensuring that the new University should be established on broad lines. It was almost entirely due to his efforts that a sum of £10,000 was raised, and thus by 1904 premises had been secured, staff recruited, and the Liverpool Institute of Archæology was inaugurated. It was Garstang who conceived and planned the Institute, it was he who made it possible, he was its honorary secretary, and retained that office for more than forty years until the independent existence of the Institute ceased with its incorporation in the University School of Archæology and Oriental Studies. In 1907 he was appointed John Rankin professor of the methods and practice of archæology in the University of Liverpool, and held the chair until his retirement in 1941.

Although each year he did a certain amount of teaching and lecturing in Liverpool, his principal interest was in excavation. His energy was immense, and every year until 1914 saw him excavating at one or more sites in the Near East. The list of sites is formidable: Beni Hasan (1902–4), Naqada, Hierakonpolis, Edfu (Hissaia) and Nubia (1904–6), Abydos (1906–9), and Meroe in the Sudan (1909–14). At Meroe he conducted the first excavations on the site and uncovered a very large section of the enormous city. Most of the results of these excavations are still unpublished; but sufficient of his records has survived to encourage the hope that in the near future it will be possible to publish reasonably full details of his results.

During these busy years Garstang found time in 1907 to make a journey of survey and exploration

across Asia Minor. This journey was to lead to an eventual widening and reorientation of his archæological interests. Apart from his own excavations at Sakje Geuzi in 1908 and 1911, in 1910 he published his book "The Land of the Hittites", which, together with its modernized successor "The Hittite Empire" (1929), was for many years the standard introduction to the subject.

In 1920, after a year as archæological adviser in Palestine, he became director of the British School of Archæology in Jerusalem, and the first director of the Palestine Antiquities Department. The creation and organization of that Department and of the Palestine Museum were virtually his own work, and showed his genius for organization at its best. Between 1929 and 1935 he directed excavations at Jericho: though some of his more optimistic claims, and still more those of over-enthusiastic supporters, are now no longer generally accepted, his work at Jericho greatly extended our previous knowledge and yielded results the importance of which cannot be disputed.

In 1936, thanks to a generous grant from Mr. Francis Neilson, he became director of the Neilson Expedition to the Near East. After a preliminary survey in Cilicia in 1936, during 1936–39 and again in 1947–48 he excavated the important site of Mersin in Cilicia. It was during his last campaign at Mersin that he was able to conduct the negotiations that led to the foundation of the British Institute of Archæology in Ankara. When the Institute was opened in 1948 he was appointed its first director, and in the following year he became its president, holding that office until his death. He died at Beirut on September 12, barely two days after his last visit to Mersin, where he had fulfilled his cherished wish to see once more the last site that he had discovered, and had addressed there a distinguished gathering.

Garstang was not a great academic figure and he built up no school of students; he was always the practical man and field-worker. He was a pioneer in many fields of archæological research. He had to an extraordinary degree a flair for discovering the good site, and once he had found that site there were few who could excel him in stimulating and sustaining general interest in the work. He had an instinctive understanding of how to appeal to the public, and his field-records and photographs show how always the propaganda side of his work was ever present in his mind. Most of his excavations, conducted in the name of the Liverpool Institute of Archæology, were carried out with the slightest of financial support: it was his gift for publicity, plus personality and untiring drive, together with loyal and generous supporters mainly in Liverpool, that year by year enabled him to open and explore new fields. It is not so much as an excavator but as an organizer that his name will live. The man whose vision and genius created organizations so diverse and so productive as the Liverpool Institute of Archæology, the Palestine Antiquities Department, and the British School of Archæology in Ankara has made a permanent contribution to archæological studies in the Near East.

H. W. Fairman

NEWS and VIEWS

Prof. Charles Singer: Eightieth Birthday

Charles Singer, historian of medicine and science, celebrated his eightieth birthday on November 2. Prof. Singer can look back on a life of striving and of achievement. His historical studies grew out of his clinical and research work. It is now fifty-one years since, returning from an expedition to Abyssinia, where he had medical and biological experience which many young men must have envied, he published his first clinical paper. There followed years of clinical work and of laboratory research, especially on gastric carcinoma. In the same week in which Fibiger announced the discovery of the parasite for which he was awarded a Nobel Prize, Singer independently discovered this parasite. He read several communications on these subjects at the International Congress of Medicine which was held in London in 1913, and that year saw the zenith of his writing on these subjects. Two years before that he had published his first historical paper, and from 1914 onwards he devoted himself to historical subjects. A short period at Oxford and some years in the R.A.M.C. during the First World War were followed by a post at University College, London, first as lecturer in, and later as professor of, the history of medicine. Though the years in London until his retirement in 1942 were full of great achievement, it is since that date that Prof. Singer has reaped his richest harvests. Besides several scholarly books which are of great importance in the history of medicine, he has contributed lavishly to a specialized branch of the history of the chemical industry, and for six years he has laboured on the monumental "History of Technology", of which he was the sole begetter, and in the production of which he has shouldered the major burden. May the approaching publication of the second volume of that five-volume work stimulate him to continue making the world his debtor.

Biochemistry in Birmingham: Prof. R. H. Hopkins

Prof. R. H. Hopkins retired from the Adrian Brown chair of malting and brewing and applied biochemistry in the University of Birmingham on September 30. A graduate of that University, he has been closely associated with the Department for many years. Thus, he was lecturer under Prof. Adrian Brown and retained that position for several years before accepting a post at the Heriot-Watt College, Edinburgh. In 1931 he returned to Birmingham, this time as head of the Department, a position he was to occupy for twenty-five years. The retirement of Prof. Hopkins may be said to close the second epoch in the history of what was originally the British School of Malting and Brewing. In the first period, 1900–20, the School was primarily concerned with these subjects; but already a wider field was being cultivated. In the earlier days of the second epoch a new pattern was being laid down, and in the research laboratories interest centred chiefly on the biochemistry of plant products, especially polysaccharides. A new building was occupied in 1927, and when Hopkins arrived in 1931 the time was ripe for further expansion. The original *raison d'être* of the Department was never lost sight of, and with the advent of a group of workers from the Institute of Brewing, fundamental work on biochemical aspects of brewing and on yeast nutrition

was actively pursued. The emphasis in the Department was changing—from static to dynamic biochemistry—never more so than in the special field of the amylases which has always claimed so much of Hopkins's time and interest. During and after the Second World War, nutritional investigations led to interest in yet another field—the vitamins of the B group, with special reference to their role in germination, malting and brewing processes, and their assay by microbiological means. An increasing preoccupation with microbiological chemistry has been observable in recent years and has resulted in useful studies in the nutrition of yeasts and bacteria. Prof. Hopkins may look back with some satisfaction on the achievements of a small department, limited in resources and with no possibility of team-work in the modern sense. Should the rumoured expansion of biochemistry in Birmingham be achieved, the Department may look forward with confidence to yet a third epoch.

Imperial College of Science and Technology, London

THE Imperial College of Science and Technology has now completed the first stage of the massive expansion being undertaken at the request of the Government. The plan, announced in 1953, is to double the size of the College to accommodate three thousand students of science and engineering. There are now 2,240 students at the College, 36 per cent more than in 1953. The number of teaching staff now stands at three hundred—a rise of 33 per cent. Twenty-seven new posts as professor or reader in the University of London have been established at the College and have been filled. They cover a wide range of subjects, from aeronautical structures, applied geophysics, instrument technology, parasitology and soil mechanics to nuclear power. A new building for aeronautics and chemical engineering is already partly in use, and will be in full operation in two months time. By this, by a reconstruction of the Students' Union and by a number of other building projects, the College has already added 20 per cent to its gross floor space. Work has now been started on the preparation of sites for large new buildings for engineering and physics.

University of Leeds

THE following have been appointed to lectureships in the University of Leeds: N. Brook (colliery engineering), Dr. A. J. Manuel (physics), J. McFarlane (mining and mine surveying), A. Peck (mine surveying) and Dr. J. E. Saxton (organic chemistry). The title of visiting professor in the University has been conferred upon Prof. Darrell Pratt, of the University of Florida, who will be working with Prof. F. C. Happold in the Department of Biochemistry during the session 1956–57. The following gifts, among others, have been received by the University: £2,000 over two years to the Department of Inorganic and Structural Chemistry from Imperial Chemical Industries, Ltd., for work on vanadium pentoxide systems; £500 a year for three years to the Department of Physical Chemistry from the Distillers Company, Ltd., for the support of research; £1,000 to the Department of Civil Engineering from the Steelwork Society for research into stress distribution of high-tensile bolted structural connexions; £3,000 for 1955–56 to the Department of Mining from the National Coal Board (North-Eastern Division); £2,000 for 1955–56 to the Department of Coal Gas and Fuel Industries from the Gas Plant Manufacturers' Development Council; £1,350 to the Department of Textile Industries from Courtaulds, Ltd.; £9,000 over three years to the Departments of Medical Physics and Radiology and Radiotherapy from the Nuffield Foundation, for research on the intensification of X-ray fluorescent screen images.

The total number of full-time students registered at the University of Leeds is now 3,731, which is some 260 more than at the corresponding date last session; of this increase, at least two hundred are in the Faculties of Science and Technology. The new admissions are about 180 more than at the corresponding date last session; 60–70 of these are on the arts side and about 120 in science and technology.

Royal Society of Edinburgh: Officers for 1956–57

THE following have been appointed to the Council of the Royal Society of Edinburgh for the session 1956–57: *President*, Prof. James Ritchie; *Vice-Presidents*, Prof. J. Norman Davidson, Principal H. B. Nisbet, Prof. Meirion Thomas, Prof. A. C. Aitken, Dr. J. E. Richey, Prof. D. Whitteridge; *General Secretary*, Prof. Norman Feather; *Secretaries to Ordinary Meetings*, Dr. T. R. Bolam and Dr. A. W. Greenwood; *Treasurer*, Mr. A. W. Young; *Curator of Library and Museum*, Dr. Douglas Guthrie; *Councillors*, Prof. E. L. Hirst, Dr. D. E. Rutherford, Dr. D. A. Allan, Prof. G. H. Bell, Dr. D. N. McArthur, Dr. A. G. MacGregor, Prof. C. H. Waddington, Dr. J. A. Macdonald, Dr. J. R. Peddie, Dr. R. Schlapp, Dr. J. B. Tait and Prof. G. M. Wyburn.

Metallurgical Reviews: a New Quarterly Journal

To all those concerned with any aspect of metallurgy, the appearance of a new quarterly periodical, *Metallurgical Reviews* (members of the Institute of Metals, 32*s*. 6*d*. or 5 dollars per year; non-members, 42*s*. or 6.50 dollars), will be of more than usual interest. Although published by the Institute of Metals, the interests of which lie in the field of non-ferrous metallurgy, the new publication will cover the whole field with the exception of mining, the extraction of metals from their ores, and practice in iron and steel works. It is intended that these reviews should be of a comprehensive and critical nature, and relate both to the industrial and the theoretical aspects of the subject. The four reviews contained in the first issue (pp. 156) fully satisfy these conditions. Prof. J.-J. Trillat (Sorbonne, Paris) has written on the metallurgical aspects of micro-radiography; Prof. C. R. Soderberg (Massachusetts Institute of Technology) on mechanical properties in relation to design requirements; D. M. Lewis (Aluminium Laboratories, Ltd.) on the principles of continuous casting of metals; and B. E. Hopkins (National Physical Laboratory, Teddington) on the preparation and properties of high-purity iron. All these are valuable compilations, very well prepared and illustrated, and on the average some sixty references are given to each section of the work. The Council of the Institute of Metals is to be congratulated on performing a most valuable service to those concerned with both the technology and the theory of metallurgy.

Two New Scottish Nature Reserves

THE Scottish Committee of the Nature Conservancy has recently established new nature reserves at Inchnadamph, Sutherland, and Glen Diomhan, Bute. The former consists of 3,200 acres south-east

of Loch Assynt and is a typical sample of west Sutherland countryside, ranging in altitude from about 230 ft. near Inchnadamph to 1,680 ft. on the summit of Beinn nan Cnaimhseag. Loch Mhaolach-coire is included within its boundaries. The reserve lies in a tract of great geological and physiographical interest, being at the western front of an area of disturbed Durness limestone of Cambrian age. At Beinn nan Cnaimhseag is an isolated outcrop of Torridon sandstone resting upon the Durness lime-stone. Although some of the limestone in the reserve is covered with acid drift and peat, much of it is exposed, and about four hundred acres consists of limestone pavements and scraps. The ground is partially covered by low willow scrub consisting mainly of *Salix myrsinites*, but also includes *S. repens*, *S. aurita* and hybrids. Mountain avens (*Dryas octopetala*) is abundant on the drier limestones, and there is a rich woodland flora of northern character including globe flower (*Trollius europaeus*) in some parts. The gorge of the Traligill Burn is well known to botanists. The karst type of limestone country with sink-holes, underground streams and limestone caves is also to be found, and the famous Allt nan Uamh bone caves contain Palæolithic cave earths with a fauna of Pleistocene mammals and traces of occupation by early man. The reserve has been established under an agreement with the owner, Mr. R. A. Vestey. The Glen Diomhan nature reserve consists of 24 acres of a steep-sided, post-glacial gorge in north-west Arran, lying between Meall nan Damh (1,870 ft.) on the west and Ben Bhiorach (1,572 ft.) on the east. The area is noteworthy for the occurrence in it of two rare whitebeams (*Sorbus arranensis* and *S. pseudofennica*), both of which are confined to Arran. They grow intermixed with rowan (*S. aucuparia*). The trees are mostly confined to a short length of the glen between the 300-ft. and 600-ft. contours and are found on both banks of the stream. The reserve has been established under an agreement with the Dowager Duchess of Montrose.

Three-dimensional and Two-phase Illustrations

The firm of Industrial Photographs, Ltd. (34 Belwell Lane, Four Oaks, Sutton Coldfield), has produced some interesting three-dimensional pictures, called 'Vectographs', in which the solid effect is produced by means of an ingenious application of polarized light. The two component images necessary for a stereoscopic picture are printed in superposition on either side of a transparent support. The nature of this support and the printing solution used results in the production of two images in which the original photographic densities are reproduced in varying degrees of optical polarization. The light passed by the first image is polarized at right-angles to that passed by the second. This composite picture is viewed through a small binocular analyser, the lenses of which are two pieces of polarizing material with their directions of polarization at right angles to one another; these lenses act as filters and are so arranged that the left and right images are visible only to the appropriate eye, thus producing a clear and striking three-dimensional effect. Three examples of subjects illustrated are the chemical structure of graphite, a shadowed carbon replica of pearlite, and a cone of *Chamaecyparis lawsonia*. By another application of the process, two different aspects of a subject are similarly superimposed. Each is visible by polarized light in one plane only, and a piece of polarizing filter (or one lens of the binocular viewer) is rotated to show either image or both, or the transition from one to the other. An example of this type of two-phase picture is one in which the two aspects are the human skull and its associated muscles and tissues. The pictures are $4\frac{1}{4}$ in. × $5\frac{1}{4}$ in. in size and are designed for educational purposes. As an alternative to passing them around the lecture-room, they can be used as slides (though they are rather large ones) and projected on to a metallized screen. Each member of the audience must, of course, have a polarizing viewer.

Antarctica Exhibition at the British Museum (Natural History)

A special exhibition on Antarctica has been arranged in the Mineral Gallery of the British Museum (Natural History) to mark the International Geo-physical Year, 1957–58 and the Trans-Antarctic Expedition. The rock specimens of the Department of Mineralogy, which form the National Collection, include many from Antarctica. Three areas have been selected for exhibition. The first area is South Victoria Land, scene of many British expeditions, culminating in those of Shackleton and Scott. South Victoria Land is now a base for New Zealand and American parties, and the final destination of the Trans-Antarctic Expedition. The second area repre-sented is Queen Maud Land, in the Norwegian section of Antarctica. Part of this territory was explored by the Norwegian–British–Swedish Expedition, 1949–52. The third area, part of the Falkland Islands Dependencies, including Graham Land and its offshore islands, is now being surveyed by many British parties. Four historical specimens displayed are: the gizzard stones of an emperor penguin taken on sea ice by Sir James Clark Ross's Expedition (H.M.S. *Terror* and H.M.S. *Erebus*) in 1849, which included rocks of continental character, and gave the first scientific evidence for the existence of a southern continent; a boulder of gneiss, a typical continental rock, dredged from the floor of the Southern Ocean by H.M.S. *Challenger* in 1874, which provided further evidence of a southern continent; rocks collected by Captain Scott's party on their return march from the South Pole in January 1912; and the Adélie Land stony meteorite, which is the only meteorite so far recovered in Antarctica. There are also photographs, paintings and maps illustrating antarctic conditions.

Michael Faraday and Spiritualism

In 1853, Michael Faraday conducted an investigation of certain spiritualistic phenomena then causing considerable stir. Using a few simple pieces of apparatus of his own design, he succeeded in establishing the same kinds of controls that characterized his more famous experimental researches and provided a rational explanation for the observed set of phenomena that was satisfactory to all. No new and strange forces were uncovered. Instead, Faraday demonstrated conclusively that the performers produced the observed effects by ordinary physical means. What was noteworthy in this inquiry—and the reason Faraday's explanation proved to be satisfactory to both sides—was that he discovered that the performers were deceiving not just others, but themselves as well. Although the performers produced the observed effects, they did so unconsciously.

Faraday investigated two sets of phenomena, the levitation of tables and the turning of tables. In his "Observations on Mental Education", which was

delivered as a lecture in 1854, he described the phenomenon of levitation. Of his investigation of the second kind of phenomena, Faraday prepared a report which was published on July 2, 1953, in the *Athenæum*, a journal devoted to English and foreign literature, science, and the fine arts, which was founded in 1828 and which continues to-day, after several mergers, as the *New Statesman and Nation*. A copy of this interesting report and some comments upon it have been set out in *Scientific Monthly* (83, No. 3; September 1956).

National Science Foundation Fellowships

THE National Science Foundation, Washington, D.C., is offering three types of fellowship awards for advanced study and research in the natural sciences during the academic year 1957–58: predoctoral fellowships for college seniors and graduates (1,600–1,800 dollars); postdoctoral fellowships for those who have already gained a doctor's degree in science (3,800 dollars); and senior postdoctoral fellowships for those who have had a doctorate for a minimum of five years and have demonstrated unusual ability for research (4,000–10,000 dollars). The awards are open to American citizens and are tenable in any non-profit institution of higher education in the United States or abroad. The fields of study may be the mathematical, physical, medical, biological, engineering and other sciences, including anthropology, psychology (other than clinical), geography, certain interdisciplinary fields, and areas of convergence between the natural and social sciences. About a thousand awards will be made and will be announced next March. Applications for predoctoral fellowships should be made by January 7, and for postdoctoral fellowships by December 24, to the Fellowship Office, National Academy of Sciences—National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D.C. For senior postdoctoral fellowships application should be made by January 14 to the Division of Scientific Personnel and Education, National Science Foundation, Washington 25, D.C.

Conference on the Biology of the Hair Follicle and the Growth of Hair

AN international conference on "The Biology of the Hair Follicle and the Growth of Hair" will be held under the auspices of the British Society for Research on Ageing at the Royal Society of Medicine during August 7–9, 1957. The Congress will deal with the gross and microscopic anatomy and histochemistry of the hair follicle and the hair, studies on mitoses of the hair follicle and effects of nutrition and hormones on hair growth, vascularity and patterns of growth, production of pigment, regeneration and *de novo* formation of hair follicles. Admission is by ticket, obtainable free of charge from the Honorary Secretary, British Society for Research on Ageing, Dr. G. H. Bourne, London Hospital Medical College, Whitechapel, London, E.1.

Announcements

DR. J. R. PRICE, senior principal research officer in the Organic Chemistry Section of the Commonwealth Scientific and Industrial Research Organization, Australia, has been awarded the H. G. Smith Memorial Medal for 1956 of the Royal Australian Chemical Institute. The Medal is for contributions over the past ten years to the development of chemical science in the field of organic chemistry and biochemistry, and the award to Dr. Price is for his researches on several types of compounds, and especially on the alkaloids.

THE Meldola Medal, which is the gift of the Society of Maccabæans, is being offered for award early in 1957 to the chemist who, being a British subject and less than thirty years old on December 31, shows the most promise, as indicated by published chemical work brought to the notice of the Council of the Royal Institute of Chemistry before December 31. Communications should be addressed to the President, Royal Institute of Chemistry, 30 Russell Square, London, W.C.1, the envelope being marked "Meldola Medal".

SIR GEORGE BEILBY Memorial awards, which are considered at intervals by administrators representing the Royal Institute of Chemistry, the Society of Chemical Industry and the Institute of Metals, are made to British scientific research workers, preference being given to investigations relating to the special interests of Sir George Beilby, including fuel economy, chemical engineering and metallurgy. In general, the awards are given to younger workers for original investigations over a number of years. For awards early in 1957, the attention of the administrators should be directed, before December 31, to work of the nature indicated, all communications being addressed to the Convenor of the Administrators, Sir George Beilby Memorial Fund, Royal Institute of Chemistry, 30 Russell Square, London, W.C.1.

DR. R. COCKBURN, deputy controller of electronics, Ministry of Supply, has been appointed controller of guided weapons and electronics in the Ministry.

MR. C. E. LAMBERT, representing the Colonial Territories, has been elected chairman of the Executive Council of the Commonwealth Agricultural Bureaux, in succession to Mr. J. E. C. Coventry, who represented the Federation of Rhodesia and Nyasaland. Lieut.-Colonel V. A. Nicholas, representing Ceylon, has succeeded Mr. Lambert as vice-chairman.

PROF. F. G. GREGORY, of the Research Institute of Plant Physiology, Imperial College of Science and Technology, London, will deliver the Amos Memorial Lecture at the East Malling Research Station, Kent, on November 15. He will speak on "The Place of Plant Physiology in Fruit-growing".

PROF. R. B. WOODWARD, professor of chemistry, Harvard University, will deliver the eighth annual Ciba Foundation Lecture on December 5 at 5 p.m. in the meeting room of the Zoological Society of London; his subject will be "Recent Advances in the Chemistry of Natural Products". Admission is by ticket only, obtainable from the Assistant Secretary, The Ciba Foundation, 41 Portland Place, London, W.1.

A ONE-DAY conference on "Automation, Education and Training" is being organized by the British Association for Commercial and Industrial Education, and will be held in the Royal Festival Hall, London, on December 4. Particulars can be obtained from the Association, at Management House, 8 Hill Street, London, W.1.

ERRATUM. In the communication entitled "Antagonists of the Action of Reserpine on Smooth Muscle" in *Nature* of October 20, p. 859, col. 2, par. 2, line 3, for "serotonin (15–40 mgm. per ml.)" read "serotonin (15–40 nanograms per ml.)".

THE DIRECTION OF RESEARCH ESTABLISHMENTS

THE scale, complexity and cost of scientific research are mounting rapidly. Laboratories are growing not only in number but also in size. To meet these ever-growing needs without waste of money or that vastly more precious commodity, scientific brain-power, a high order of organization and management is required. This is a comparatively new problem of administration—research has developed into a large-scale industry only in the past few decades—and there are almost no precedents in any field of human endeavour for showing the large-scale organization of mental and imaginative creativeness as a team effort.

The direction of research establishments was the subject of an international symposium organized by, and held at, the National Physical Laboratory during September 26–28. Delegates from seventeen countries attended. They were mainly directors of large laboratories—government, industry and public corporations—with a small representation of universities. Attendance was severely limited to 150. Papers were circulated before the conference, so that most of the conference time could be devoted to discussion.

The general plan of the symposium was that the first day should be devoted to choice of project, general problems of organization and control of research, and the personal and social factors affecting creativity in scientists. The second day provided three parallel sessions on general organization, staff and communication. The third day started with reports from, and joint discussion on, the previous day's sessions, followed by consideration of the assessment of the work of a research laboratory and a general summing up.

The proceedings were opened by Dr. G. B. B. M. Sutherland, who had just previously taken up his appointment as director of the National Physical Laboratory. The first session was then devoted to the strategy of research and the choice and termination of research projects. Prof. J. D. Bernal introduced a thought-provoking paper on "Fundamental and Applied Aspects of Research Problems". In this he emphasized that finding the problem is much more difficult than finding the solution. It is not the problem but the particular need or difficulty that stands out. It is necessary, therefore, before research is started, to reduce the immediately perceivable gap between what is known and what is required to something which can be measured scientifically. He described the working of various types of research laboratories and suggested that one of the most important aspects of the integration of research is that subsidiary problems should be referred to appropriate organizations such as research associations or national laboratories.

In dealing with invention, Prof. Bernal pointed out that its history shows that actual success depends not only on originality and imagination but also on knowing what to invent, that is, on a knowledge of requirements and of market possibilities and costs and prices. The frequent practice of firms in not allowing employees to profit directly from their invention was described as being the 'best way of killing the goose that lays the golden egg'. Prof. Bernal also thought that scientists tend to work too long on lines of traditional, set problems, whereas major advances have occurred when this rule is broken. He advocated a closer liaison between industrial and university research workers as providing two-way benefits.

The other paper in this session was by Dr. Willis Jackson, on "The Research Project—Its Choice and Termination". In this, comparisons and contrasts were drawn between the factors governing the initiation and termination of research in universities and in industry, although the outlook, approach and method of the true research worker were stated to be the same whatever his setting.

Dr. Willis Jackson gave various examples of work originating in individual inspiration which had extensive technological consequences not originally envisaged. He pointed out that the industrial research laboratory is fortunate in having ready access to the wider environment of a range of design and manufacturing activities as an outlet for its personnel. For this and other reasons he regarded it as essential for all industrial research recruits to spend a training period in carefully chosen departments of the main factory.

The first part of the second session was devoted to consideration of creativity. "Creativity and the Scientist" was introduced by Prof. Morris Stein, of the University of Chicago, and "Personality and Social Factors related to Creativity", by Prof. D. J. van Lennep, of the State University, Utrecht.

Prof. Stein surveyed the work of his team on the sociological and psychological factors related to creativity in industrial research chemists. The object of this work is the understanding of the processes involved in creativity so as to facilitate the selection of creative scientists and the administration of creative research. He stated that creativity is a process of hypothesis formation, hypothesis testing and communication of results, and that scientists can be creative in either or all of these fields. He stressed that there are differences between scientists working in different fields and in different environments, and advised employers to have a clear picture of the kind of man they want before starting to look for creativity.

Prof. van Lennep made a preliminary division of research workers under three categories: need for achievement, problem-solving ability and creativity; and he pointed out that a large research laboratory must have staff of each type. For physicists and chemists he postulated that creative workers are less dependent with respect to their environment; are less rigid and dogmatic and have a characteristic time perspective.

The final paper in this session was given by Mr. D. R. Willson, technical secretary of the Atomic Energy Research Establishment, Harwell, on "Budges and Administrative Controls". He discussed the needs for budgets and controls in research and development establishments, and how those which are essential can best be applied.

The general organization session started with discussions of a paper by Mr. E. S. Hiscocks, secretary of the National Physical Laboratory, on "Some

Factors affecting Laboratory Administration". In this paper Mr. Hiscocks dealt first with the changed requirements caused by the transition of research from a craft to a large-scale industry. The effects of size on the organization were then examined and the great need for devolution stressed. The division of work in large laboratories was next considered, as were also the effects on their staffing and organization of large-scale, expensive equipment.

The next paper, on "Science and the Workshop", by Dr. R. Vieweg, president of the Physikalisch-Technische Bundesanstalt, was presented by Dr. A. Scheibe, his vice-president. This discussed the place of workshops in laboratories and the types of shops and their organization to meet the requirements of modern research. This raised the controversial question of the degree of centralization of services required to produce optimum results.

The afternoon of this group session was devoted to laboratory buildings. Dr. F. M. Lea, director of the Building Research Station (Department of Scientific and Industrial Research), outlined the requirements and Mr. H. A. Snow, superintending architect, Ministry of Works, gave the architect's answer to these demands.

Punch remarked, more than twenty years ago, that the greatest of all the research problems is the people who do the research, and this was shown to be still the case by the discussions of the staff group. Dr. W. S. Bristowe, head of the Central Staff Department, Imperial Chemical Industries, Ltd., and Dr. F. T. Rosser, director of administration, National Research Council of Canada, presented papers on selection and personal assessment of staff. Dr. Rosser's account of what he described as "fantastic" methods used by employers in Canada to obtain scientists caused considerable comment in the daily press. Prof. H. A. Shepard, of the Massachusetts Institute of Technology, next discussed "Superiors and Subordinates in Research", and described the new orientations that have emerged from the work of sociologists in this field over the past twenty-five years. Prof. Shepard has himself made a significant contribution to these studies. Sir Charles Harington, director of the National Institute for Medical Research, then introduced the subject of "Staff Groupings and the Flow of Authority". The last subject discussed in this session was "Incentives". This was introduced by Mr. Stanley Mayne, secretary of the Institution of Professional Civil Servants. It was a refreshing experience for the 'managers' to hear the views of the 'managed' on this very important subject.

The third group session—that on communications—dealt first with internal communications in a large research laboratory and was introduced by Dr. C. G. Williams, director and general manager of 'Shell' Research, Ltd. This was followed by a paper "Studies in the Use of Technical Information in the Smaller Industrial Establishments", by Mr. Louis Moss and Mr. L. T. Wilkins, of the Central Office of Information. This paper described a statistical survey recently made into the dissemination of technical information in industry; and preliminary results of an investigation of the electrical and electronics industry in Great Britain were presented for discussion by Mr. Geoffrey Thomas in the unavoidable absence of Mr. Moss.

Dr. A. T. Green, director of the British Ceramic Research Association, presented a paper by himself and Dr. A. E. Dodd, information officer of the Association, on "Knowledge: Passing it on—Getting it used", and Mr. A. J. Garratt, liaison officer of the National Physical Laboratory, dealt with problems of "Extramural Communications".

Mr. M. W. Thistle, chief of the Public Relations Branch, National Research Council of Canada, presented, in his inimitable style, the last paper in this group, on "Some Fundamental Difficulties in Popularizing Science". He contended that although only perhaps 0·01 per cent of information of a highly sophisticated nature can in fact be communicated to an unsophisticated audience, the amount of information emanating from science is such that the quantity ultimately absorbed is still significant.

Dr. D. W. Hill, director of the Shirley Institute, Didsbury, was chairman of the session on general organization, Dr. J. Bronowski, director of the Coal Research Establishment of the National Coal Board, was chairman of that on staff and Dr. A. King, Department of Scientific and Industrial Research, of that on communication. These chairmen presented to the complete conference next morning admirably lucid and stimulating summaries of the previous day's discussions.

The final session considered a paper on the assessment of the work of a research laboratory by Mr. A. H. Wilson, managing director of research and development, Courtaulds Ltd., and chairman of the Industrial Research Committee, Federation of British Industries. Mr. Wilson pointed out that the standing of an academic laboratory depends largely upon subjective judgments—the æsthetic appeal of its results to the general body of academic scientists—whereas in the industrial world a laboratory is of no importance unless it exerts a positive influence on its industry, and this, ideally, is capable of measurement. On the subject of stopping research, Mr. Wilson advocated the early and continuous assessment of the whole project and its consequences—a process in which the research worker must take part and the consequences of which he should, therefore, accept. Discussion on this paper and on the conference in general was opened by Dr. A. V. Astin, director of the National Bureau of Standards, Washington.

A summing up of the conference was then given by Dr. H. W. Melville, secretary of the Department of Scientific and Industrial Research, who was chairman of this session.

It is impossible in an article of this length to summarize the many points of view put forward; but it became evident that many of the major problems of large-scale research are fundamentally the same whatever the country and whether the research is on behalf of government or industry. It was also surprising that the solutions evolved by apparently widely differing organizations bear close resemblances. This applies particularly to general organization of research services, and to the broad problems of the selection and personal assessment of staff. However, one of the major difficulties of the government research institution—what to do with the research scientist who has become less productive—is not shared to anything like the same extent by industry, where young men from the research department are continually transferred to other branches of the industry, such as technical sales, production, control, etc. The problems of internal communication are broadly similar whatever the type of industry and naturally increase with the size of the institution; but here again industry is not faced with many of the problems of external communication that are

major concerns of government research for the civilian economy.

Although most of the participants in the symposium and many of the contributions came from those actually engaged in directing or administering large research establishments, considerable interest was shown in the 'research into research' papers, such as those from the psychologists, sociologists, statisticians and the trade union side. It is now clear to many research directors that, to borrow a phrase from Dr. Ellis Johnson, we should have more "operations research looking at research operations".

A surprise to the organizers of this symposium was the large number of people from many parts of the world who wished to attend, and it has become clear that discussion of problems such as those dealt with, and of the many more which time did not permit to be raised, must continue. The form which this follow-up and possible extension should take is now under consideration.

All papers presented at the symposium and summaries of the discussions will be published as soon as possible by H.M. Stationery Office, London.

E. S. Hiscocks

INTERNATIONAL SOCIETY OF BIOCLIMATOLOGY AND BIOMETEOROLOGY

THE first business and scientific meeting of the International Society of Bioclimatology and Biometeorology was held at Unesco House, Paris, during August 29–31. Approximately sixty members, representing sixteen nations, were present. The major items covered included the drawing up of a set of statutes; the election of an executive board and a governing council; the introduction to members, through a series of area reports, of the various aspects of bioclimatological research in progress in different parts of the world; and the presentation of a small number of scientific papers.

Bioclimatology is not a new science, nor is it yet a unified one. The scope of the subject was brought out at the Paris meeting, and it speaks well of the new Society that its prime purpose should be to "unite . . . all Bioclimatologists working in the fields of Medical, General Botanical, Agricultural, Forest, General Zoological, Veterinarian, Entomological and Cosmic Bioclimatology and other future branches of Bioclimatology, . . . to facilitate the development of Bioclimatology". To achieve these ends it proposes to organize symposia, create a clearing house for publications, inaugurate a journal, institute subcommittees in specialized fields and, so far as possible, obtain funds for the fostering of research. The administration of the society is under the ægis of an executive board of seven members, assisted by a governing council of twenty-five. The following were elected to the executive board: *President*, Dr. F. Sargent (United States); *Vice-Presidents*, Prof. H. Berg (Germany), Dr. H. Boyko (Israel) and Prof. L. Emberger (France); *Secretary-Treasurer*, Dr. S. W. Tromp (Netherlands); and *Advisory Members*, Mr. W. E. Arnould-Taylor (Great Britain) and Dr. W. G. Wellington (Canada).

A total of seven area reports briefly described the work of individual bioclimatologists in North America, Western Europe, Africa, South-East Asia and Israel. Such a review provided an excellent, up-to-date account of research in progress. In addition, the width and variety of interests within the subject were made apparent through these reports, as can be seen from the inclusion of such topics as: asthma and hay-fever studies in relation to pollen, fungi and meteorological conditions of the atmosphere; the influence of climate on the behaviour and survival of forest insects; the use of weather data in connexion with irrigation; and a study of problems of clothing and resistance to extreme climates arising from pilgrimages by sea and land to Mecca.

Four sub-committees were instituted, the function of which is to collate and disseminate information on the respective specialized fields of ionic research in bioclimatology, allergy, ecological climatology and bioclimatological instruments. A proposed fifth subcommittee on nautical bioclimatology was referred to the executive board for further consideration.

It was proposed to hold a second meeting of the Society in Vienna in 1957, although a subsequent annual periodicity is not necessarily to be inferred. However, the Paris meeting showed many potential attenders to have been pre-occupied with earlier commitments, and lacunæ in some area reports suggest that scientists in certain areas and disciplines may not have fully realized the extensive nature of the Society's intentions. For these reasons and others, an early re-assembly appeared desirable.

The Society largely owes its inception to the initiative of Dr. S. W. Tromp, who got into touch with bioclimatologists in different parts of the world during the previous twelve months and also played a major part in the organization of the Paris meeting. His acceptance of the secretaryship, which he will conduct from 54 Hofbrouckerlaan Oegstgeest, Leyden, is a fortunate event for the Society.

M. J. Delany
F. L. Waterhouse

YEAST IN INDUSTRY

UNDER the joint sponsorship of the Dublin and District Section, the Microbiology Group and the Food Group of the Society of Chemical Industry, a symposium on "Recent Studies in Yeast and their Significance in Industry" was held in Dublin during September 17–19. The sessions were held in the Rupert Guinness Hall by kind invitation of Arthur Guinness Son and Co. (Dublin), Ltd., on behalf of whom Sir Richard Levinge welcomed the 125 members of the symposium; some seventy-five members attended from overseas. The basis of the symposium was provided by thirteen papers, the reading of which was followed by lively discussions in which many members participated. The chair was occupied in succession by Mr. H. J. Bunker, Prof. T. Dillon, Dr. A. K. Mills, Dr. A. J. Amos and Dr. L. A. Allen.

The first paper, by Dr. A. A. Eddy (Brewing Industry Research Foundation), dealt with "Some Chemical Aspects of Yeast Growth". First, Dr. Eddy described the use of media containing L-lysine as sole major source of nitrogen for the isolation of wild yeasts and the estimation of the extent to which they contaminate brewery pitching yeasts. He then discussed three commercially important aspects of the behaviour of yeasts, namely, head retention, flocculence and finability, which are associated with the surface structure of yeast. In particular, he

indicated how these aspects may vary from strain to strain and suggested the division of yeasts with respect to flocculence into those which (*a*) flocculate under the influence of chemical factors (sugars, *p*H, ethanol); (*b*) undergo mutual flocculation; and (*c*) are non-flocculent.

Presenting a paper on "Inositol Deficiency in Yeast with Particular Reference to Fat Production" on behalf of S. W. Challinor, N. W. R. Daniels and J. C. Hall (University of Birmingham), Dr. Challinor reported that the fat content of the cells of a brewer's yeast is greatly increased by growth in a medium deficient in inositol. The possible commercial value of this phenomenon is enhanced by the fact that such fatty, inositol-deficient cells are also more fragile than are normal cells, so that extraction of fat is facilitated.

In his paper on "Amylase Systems in Brewery Yeasts", Prof. R. H. Hopkins (University of Birmingham) pointed out that, although glucose, maltose and maltotriose are the only sugars of the starch series fermentable by them, brewer's yeasts elaborate (*a*) a debranching enzyme ('isoamylase') which splits α-1.6-linkages in branched structures such as amylopectin and its β-limit dextrin, and (*b*) a branching enzyme which transforms the straight-chained amylose into a branched compound. Yeasts which ferment starch and dextrin may occur as contaminants in the brewery. Such is *Saccharomyces diastaticus*, which secretes glucamylase (amyloglucosidase) at or near the cell surface. This enzyme splits successive terminal glucose residues from α-1.4-linked polyglucosans to yield β-glucose. Infection by *Sacch. diastaticus* may therefore cause 'super-attenuation' in bottled beers. In other circumstances, *Sacch. diastaticus* is potentially useful for producing ethanol from starchy materials and for carrying further the attenuation of beers.

Mr. F. W. Beech (Long Ashton Research Station) spoke on "Yeast Control in Cider Fermentation". The inoculum which initiates the fermentation of apple juice is provided by the natural microflora of the fruit. After outlining the changes in the yeast populations of fermenting ciders, Mr. Beech discussed some methods of microbiological control. Thus, a French method consists in reducing the nitrogen content of the juice. In England, aerobic spoilage organisms may be suppressed by keeping fermenting and stored ciders under anaerobic conditions, the yeast population being controlled simultaneously by mechanical methods. Sulphur dioxide, added to the original juices, effectively controls both yeasts and bacteria.

Two prominent Continental scientists provided papers to illuminate those little-understood, but fundamental, aspects of yeast behaviour which centre around the phenomenon known as the 'Pasteur effect'. Dr. H. Holzer (University of Hamburg), in his contribution, "Regulation of Carbohydrate Metabolism in Yeast Cells", adduced evidence for the theory that the key enzyme system affected by the change from anaerobic to aerobic conditions is that catalysed by triosephosphate dehydrogenase, the action of which depends on the available adenosine diphosphate and orthophosphate. Thus, there is a decrease in concentration of orthophosphate associated with the functioning of terminal respiratory processes brought into action when oxygen is introduced into a system fermenting under the action of living yeast. The resultant limitation of supply of orthophosphate will therefore restrict glycolysis. Ultimately, the Pasteur effect appears to be associated with a shift of adenosine triphosphate from the cytoplasm to the mitochondria. Dr. Holzer also discussed the occurrence of aerobic fermentation in connexion with growth. Aerobic fermentation increases when ammonium salts are added to yeast cells which are oxidizing glucose. In these circumstances, the increase in cell substance is largely due to the amination of α-ketoglutarate to glutamate catalysed by glutamic acid dehydrogenase in the presence of coenzyme I. This enzyme and the transaminase catalysing the formation of aspartate from glutamate and oxalacetate are present in yeast.

An obverse aspect of the Pasteur effect was presented by Dr. P. P. Slonimski (University of Paris) in his paper, "Respiration and Growth of Yeasts", in which he described studies involving respiratory mutants and the measurement of cell synthesis under anaerobic and aerobic conditions. *Growing* baker's yeast, even if aerated, ferments glucose: in the exponential phase, respiration is weak, the Pasteur effect is inoperative and ethanol accumulates. In this phase cytochrome synthesis is inhibited by glucose fermentation (the 'counter-Pasteur-effect'). Only in the last phase of growth, when "yeast dissimilates the alcoholic products of its own dissipation", is ethanol respired. Apart from his main thesis, Dr. Slonimski directed attention to a serious systematic error caused by absorption of carbon dioxide in work involving the measurement in conventional manometric apparatus of oxygen uptake when the ratio of carbon dioxide evolution to oxygen uptake is large, as is indeed the case with yeast. He also reported a requirement for ergosterol shown by yeast growing under strictly anaerobic conditions.

In passing, it would appear that some of the work described by Drs. Holzer and Slonimski supports the contention that the pathways of aerobic and anaerobic dissimilation in yeast are common at least up to the pyruvate stage.

Reading the paper by P. F. E. Mann, W. E. Trevelyan and J. S. Harrison (Distillers Co., Ltd.) on "Measurement of Levels of Metabolites within the Yeast Cell during Fermentation", Mr. Mann described the application of ion-exchange resins to the analysis of heat-killed yeast for intermediates and coenzymes. Such analyses promise to yield important information concerning the mechanism of regulation of the fermentation cycle. After a routine of elution has been established, separations are effected and fractions are analysed by simple techniques including measurements of ultra-violet absorption and estimations of total hexose, pentose, fructose and total phosphate. The quantitative results support the hypothesis that the enzymes which catalyse the reversible reactions of fermentation are in excess, so that, at the steady state of fermentation, their substrates are in equilibrium. Furthermore, in a simple medium, the saturation of carboxylase by its substrate, pyruvate, imposes on the rate of fermentation an absolute limitation which can be lifted by addition of thiamine. The high metabolic activity of trehalose and trehalose phosphate during the early stages of fermentation, as noted by these workers, is strong presumptive evidence that these substances play important parts in the metabolism of yeast.

Prof. E. J. Conway (University College, Dublin) contributed a paper on "Active Transport across the Yeast Cell Membrane", a subject with which his name is inseparably connected. He described how the

material requirements of yeast enter the cell largely as a result of active transport during fermentation, a process requiring energy derived from other systems and effected by means of carriers, the general cationic carrier being a redox carrier of the cytochrome type. The affinity of the carrier for potassium ions is much greater than that for sodium or magnesium ions.

Aspects of yeast genetics were dealt with in two papers which followed the showing of the film, the "Life Cycle of the Yeast Cell", made for the Anheuser-Busch Co., with a commentary by C. C. Lindegren. Mr. R. B. Gilliland introduced the film and followed with a paper on "Yeast Genetics in Industry". He said that, as yet, the application of the technique of breeding yeasts for the purposes of brewing beer is disappointing, partly because of difficulties inherent in a yeast-breeding programme and partly because the assessment of desirable qualities is so difficult. The situation with respect to other yeast industries appears to be more hopeful, and the possibilities of polyploid yeasts have yet to be examined. On the more positive side, the study of yeast genetics has accumulated valuable data on the inheritance of the ability to flocculate and to ferment maltotriose, dextrin and starch. In more academic fields, the genetic analysis of yeast hybrids may find use in the separation of yeast enzymes.

In a paper on "Some Genetical Aspects of Panary Fermentation", Mr. R. R. Fowell (Distillers Co., Ltd.) presented the results of fermentometer tests on standard doughs fermented by yeasts obtained by breeding in a scheme which permitted subsequent genetical analysis. The results for the 1 hr. volume tests can be explained in terms of four major genes operating for dominance, but those for the 1–3 hr. test are complicated by action of genes operating negatively. He concluded that detailed genetical analysis of the haploid parents is necessary before the panary performance of individual hybrids could be predicted.

"The Utilization of Flour Sugars during Panary Fermentation" was discussed by Dr. R. R. McKenzie (Distillers Co., Ltd.). The subject had been studied by the application of quantitative paper chromatography to that fraction of flour extracted by aqueous ethanol. The observed changes in concentration of glucose, sucrose, glucodifructose and lævosine during fermentation were presented and their significance discussed.

The final paper, by Dr. J. White (Fardon's Vinegar Co., Ltd., Birmingham), on "Influence of Environmental Factors upon Yeast Behaviour", urged a greater appraisal of environmental effects as a step towards the production of yeasts of high fermentative capacity and good keeping qualities. The importance of such effects was illustrated by reference to the phenomenon of 'osmosensitivity', the conditions for which are developed by growth of yeasts in direct culture, but not by growth under conditions of incremental feeding. Dr. White also discussed the change in enzyme content of yeasts in relation to the capacity to ferment glucose and maltose and to secrete invertase. The enzyme content is often influenced both by the stage of harvesting of the yeast and by the nature of the sugar present in the medium.

The final summing up of the symposium was made for the brewing industry by Dr. A. H. Cook (Brewing Industry Research Foundation) and for the baking industry by Dr. J. B. M. Coppock (British Baking Industries Research Association). Dr. Cook pointed to the recent upsurge of yeast research, but also indicated the gulf which still separates pure research from the reality of technological practice. Dr. Coppock directed attention to the new questions posed as a result of every scientific advance. Both speakers brought out the value of work ostensibly carried out in one field to work in another field: in particular, the 'cross-linking' between brewing and baking had manifested itself in this symposium.

Perhaps it was surprising that no paper devoted to questions of the fundamental nutrition of yeast was presented. Such questions, of course, arose incidentally; but it is to be hoped that this deficiency does not reflect a neglected aspect of yeast research. For all that, the symposium was undoubtedly most successful: the amount and vigour of the discussion succeeding each paper testified to the interest aroused at this most informative and stimulating meeting. It is also necessary to add that splendid organization and generous hospitality, for the major part of which the symposium was deeply indebted to the firm and staff of Arthur Guinness, Son and Co. (Dublin), Ltd., contributed substantially to its success.

C. Rainbow

FREE RADICALS

SYMPOSIUM OF THE CHEMICAL INSTITUTE OF CANADA

A SYMPOSIUM on recent progress in the production, isolation and identification of free radicals was held during September 10–11 in the Chemistry Department of Laval University, Quebec. The meeting was sponsored by the Physical Chemistry Division of the Chemical Institute of Canada, and the arrangements were made by Dr. J. A. Morrison (National Research Council) and Prof. P. A. Giguère (Laval University).

The first group of papers dealt with spectroscopic studies of radicals produced by flash photolysis or shock waves. The paper by Drs. G. Herzberg and J. Shoosmith (National Research Council, Ottawa) discussed the CH_3 and CD_3 radicals. Although their spectra are predissociated, the structure of the CD_3 band at 2140 A. indicates that one state, probably the upper, is planar with $r_0(CD) = 1{\cdot}072$ A. and that the other state is slightly bent. Further work is in progress with the view of finding a predicted 'forbidden' transition in the visible which would not be predissociated.

Prof. G. Porter (University of Sheffield) presented a paper showing that simple aromatic radicals such as benzyl can be observed in vapour phase and in solution using flash photolysis, as well as in rigid media at low temperatures. He cited recent work by Bridge and Porter on the photochemistry of quinones in solution, where triplet states, semiquinone radicals and radical ions have been observed and their reactions studied.

Two papers from the National Research Council (Ottawa) dealt with triatomic radicals. In the first of these, Dr. D. A. Ramsay discussed the spectra of HCO, NH_2 and PH_2, all of which show long progressions of the bending vibration ν_2 due to a large difference in bond angle between the upper and lower states. The NH_2 radical has a $^2B_1$ ground state with $r(NH) = 1{\cdot}025$ A. and a bond angle of 103°. Its upper state is linear, probably $^2\pi_u$, and

provides the first example of the interaction of the electronic angular momentum and the vibrational angular momentum of the bending mode of a linear molecule which was predicted by Renner. For PH_2 and PD_2 the bending vibrational interval in the upper state is found to pass through a minimum with increasing vibrational quantum number (v'_2). This is thought to be due to steric repulsion of the hydrogen (or deuterium) atoms at large vibrational amplitudes. The second of these papers was presented by Dr. F. W. Dalby, who showed that bands near 7500 A. tentatively assigned to DCO by Herzberg and Ramsay are due to DNO. Bands due to HNO in this region of the spectrum and lasting up to 1/10 sec. have been obtained in the flash photolysis of nitroethane, amyl nitrite and ammonia plus nitric oxide.

The only paper describing shock-wave techniques was given by Dr. N. Davidson (California Institute of Technology), who has studied the decomposition of nitrogen pentoxide in an excess of argon. In this system he was able to photograph the absorption spectrum of the NO_3 radical and to measure the rate constants of the following reactions:

$$N_2O_5 = NO_3 + NO_2$$
$$NO_3 + NO_3 = 2NO_2 + O_2$$
$$NO_3 + NO_3 = NO_2 + O_2 + NO$$

The discussion of these papers brought out both the relative advantages and limitations of these techniques and of work in rigid media, the conclusion being that they were complementary to each other.

The second group of papers dealt with the mass-spectrometric detection of free radicals and atoms produced in a variety of ways. Drs. W. A. Bryce, D. J. Fabian and K. U. Ingold (University of British Columbia) used the pyrolysis of mercury dimethyl to produce methyl radicals which reacted with oxygen in a quartz vessel designed to eliminate the need of a carrier gas. CH_3, CH_2, CH_3O_2, CH_3O, OH and HO_2 were among the radicals detected. In his paper, Dr. F. P. Lossing (National Research Council) described the detection of free radicals in the mercury photosensitized decomposition of acetaldehyde, acetone, ethylene, etc., using a flow system; by varying the length of the irradiated zone it was possible to distinguish between primary processes and secondary reactions. Dr. Lossing also showed that recent calculations of free-radical ionization potentials by Dr. J. A. Pople were in good agreement with the experimental values.

The electric discharge was the source favoured by Drs. S. N. Foner and R. L. Hudson (Johns Hopkins University) and by Drs. J. Herron and H. I. Schiff (McGill University, Montreal). The former have studied the formation of the HO_2 radical in a variety of systems and have found that an important homogeneous reaction is

$$OH + H_2O_2 = HO_2 + H_2O$$

The latter have studied the reaction of oxygen atoms with various species and find a rate constant of 3×10^{10} ml. mole^{-1} sec.$^{-1}$ for bimolecular reaction with nitric oxide.

The papers by Drs. P. LeGoff and L. P. Blanchard (University of Nancy) and Dr. A. J. B. Robertson (King's College, London) discussed processes occurring on hot metal surfaces in the presence of gases at low pressures. The former authors observed such species as CCl_2 from CCl_4 and CS from CS_2. Dr. Robertson discussed the adsorption of ethane and oxygen on platinum surfaces, and showed that the decomposition of the former was not in accordance with the transition-state theory. This point was further brought out in discussion, as was a general agreement over the mechanism of the formation and removal of the HO_2 radical which is still eluding the spectroscopists. Dr. C. K. Jen (Johns Hopkins University) reported unsuccessful searches over a wide range of the microwave region, and, in a later paper, Prof. P. A. Giguère and Dr. K. B. Harvey (Laval University) reported their failure to date to obtain the infra-red spectrum of HO_2 at low temperatures by condensing the products of a discharge through water vapour.

The next two papers described work at the National Bureau of Standards (Washington, D.C.) on the products from a microwave discharge through nitrogen collected on a surface at liquid-helium temperature. Dr. A. M. Bass discussed the experimental side of the work, the most striking feature of which is a green glow from the condensed solid with a half-life of about 15 sec. after the discharge has been switched off. Dr. C. M. Herzfeld showed that this spectrum arises from the $^2D \rightarrow {}^4S$ atomic transition of nitrogen, the position of which is shifted by the presence of molecules within one or two angstroms. Also present are bands attributed to a $^5\Sigma_g^+ \rightarrow A\,^3\Sigma_u$ transition of N_2, the $^5\Sigma$ state arising from normal atoms and having a very shallow minimum. Dr. G. C. Pimentel (University of California, Berkeley) described infra-red studies of radicals trapped during the photolysis of hydrazoic acid in an inert matrix at 30° K. There is strong evidence for NH_2 and N_3 radicals in this system. This produced a lively discussion, and Pimentel's work agrees with that of Dr. B. A. Thrush (Cambridge), who has found the ultra-violet absorption spectra of N_3, NH and NH_2 in flash photolysis of hydrazoic acid. N_3 was probably absent in the work at the Bureau of Standards, as its ultra-violet spectrum was not observed. It is surprising that N_3 is not formed from a metastable N atom and an N_2 molecule in this system; but Herzfeld has estimated the binding energy of the atom to be only a few hundred wave-numbers.

Dr. P. Smith (Purdue University, Indiana) presented evidence from various sources for the existence of the HO_3 radical and H_2O_4. No one present had any direct experimental evidence of these species.

The last three papers dealt with paramagnetic resonance. Dr. R. Livingston and H. Zeldes (Oak Ridge, Tennessee) pointed out the importance of using single crystals if trapped radicals were to be positively identified in irradiation experiments at low temperatures. They had, however, good evidence for OH radicals in the glass obtained by condensing the products of a discharge through water vapour. Drs. C. K. Jen, S. N. Foner, E. L. Cochran and V. A. Bowers (Johns Hopkins University) studied the products condensed from a discharge through hydrogen at liquid-helium temperatures. They found two triplets and a quartet near the free-electron resonance, and suggested that these might be due to H_3 or triplet H_2.

Dr. J. E. Wertz (University of Minnesota) discussed the hyperfine structure of the resonance spectra of semiquinone radicals; this is determined by the number and distinguishability of the protons present in the radical and greatly facilitates identification of the steps in quinone reactions. The dis-

cussion showed that this technique had great sensitivity and could well be applied to short-lived species.

The credit for the success of the meeting must be shared between the organizers and the authors of the nineteen papers presented, which dealt with very recent advances in fields that were, almost without exception, completely unknown ten years ago.

B. A. Thrush

INSPECTION OF INDUSTRIAL POLLUTION IN BRITAIN

REPORT FOR 1955

THE ninety-second report on alkali, etc., works in England and Wales and in Scotland by the chief inspectors, covering 1955*, records 921 works in England and Wales registered under the Act at the end of the year, operating 1,794 processes, which is a decrease of six in the number of works and an increase of ten in the number of processes. The 3,894 visits and inspections made during the year included 165 special visits by the chief and deputy chief inspectors; of the total, 521 visits were to or in connexion with works not registered under the Act, and a further 60 visits were to or in connexion with colliery spoil-banks. During the inspections, 2,057 quantitative analyses were made of gases evolved from processes in operation, and 827 special samples were submitted for detailed examination to the Government Chemist. Complaints and requests for technical advice and assistance involved a hundred registered and ninety-four non-registered works, the corresponding figures for 1954 being seventy and ninety, respectively; the increase is attributed not to deteriorated conditions but to a greater public awareness of the desirability of cleaner air. During the past few years there has been an increase in what are conveniently termed "area complaints", the complaint being directed against emissions from a highly industrial area or one of intensive production, such as Trafford Park, Manchester, and the Thamesside cement area, rather than against that from individual works.

On twenty-one occasions the total acidity of gases escaping to the atmosphere exceeded the statutory limits, and a further twenty-seven infractions related to failure to use "best practicable means". Since on formal notification of infraction suitable action ensued, there was no occasion to institute proceedings. Visits were paid both to the oil-fired Bankside and the coal-fired Battersea electricity generating stations, both of which are in London, to assess the efficiency of the installations for washing flue gas. While the position at Bankside was most satisfactory, the problem at Battersea is more difficult and has to contend with a doubling of the ash content of the coal since before 1939.

The high demand for cement has continued, and all kilns have operated at full output even when their associated dust-arrestment plants are undergoing repair, so that it was not surprising, especially in view of the fine summer, that there were complaints from most cement-making areas. The inspectorate continued its general policy of ensuring that all de-dusting plant is kept in as efficient a state as possible, that shut-downs are kept to the absolute minimum and that standards of supervision and "housekeeping" are as high as possible. The operation and maintenance of electrical precipitators still give real difficulty at many works. The production of sulphuric acid as monohydrate reached a record in Britain of 1,899,000 tons, an increase of 61,000 tons over 1954, and there was a spectacular increase in the usage of anhydrite for the dual production of sulphuric acid and cement clinker—from 177,000 tons in 1954 to 382,000 tons—and this process involves a serious problem of mist in the final escapes to air.

The Chief Inspector for Scotland reports no change in the number of works (82) registered under the Acts; but the number of processes operated increased by three to 119. On the 195 visits made to registered works, 92 chemical tests of flue emission were made involving the analysis of 116 samples, 14 by the Government Chemist; a further 166 visits were made which were not directly related to the provisions of the Acts. The Chief Inspector remarks that recent research has thrown more light on the dispersal of gases and dust from chimneys, and it seems desirable that the results of this work should be applied more generally, if only to test their validity; he cites an instance in which recently published work on dispersal of dust from high chimneys was particularly useful in connexion with dust emission from a power station in the west of Scotland which is fired with pulverized fue'.

* Ministry of Housing and Local Government; Department of Health for Scotland. Alkali, etc., Works Regulation Act, 1906, and Alkali, etc., Works Orders 1928–1950. Alkali, etc., Works Regulations (Scotland) Acts, 1906 and 1951. Ninety-second Annual Report on Alkali, etc., Works by the Chief Inspectors, 1955. Pp. 51. (London: H.M.S.O., 1956.) 2s. net.

BIRD SEMANTICS

MOST birds have a rudimentary language. A crow, for example, gathers its flock by uttering a distinctive 'assembly call' and disperses it by squawking an 'alarm call'. The flock will respond to tape recordings of these calls just as it does to the cries of a live bird.

Two research groups, one in the United States, the other in France, recently exchanged tapes on which they had recorded the calls of their native crows. Their object was to learn whether French 'crows' (rooks, jackdaws and carrion crows) would understand the language of the American eastern crow, and vice versa (*Sci. Amer.*, August 1956). Roosting French 'crows' consistently ignored the alarm call of American crows; but more than half the French birds were aroused by the broadcast of an American 'gathering' call. American crows were wholly unmoved by the plaintive cries of nestling rooks or the strident assembly call of adult jackdaws—commands which all three species of French crow invariably obey.

In a further experiment, the French investigators broadcast the food-finding and alarm calls of the American herring gull, a bird that also dwells on French coasts. The French gulls paid no heed to the American calls. From these experiments the investigators concluded that birds learn the language of their kind from older birds of their own group. The investigators included R.-G. Busnel, J. Giban and Ph. Gramet, of the French National Institute for Agricultural Research; the Americans were Hubert and Mabel Frings and J. Jumber, of Pennsylvania State University and the Mount Desert Island Biological Laboratory.

PAN INDIAN OCEAN SCIENCE CONGRESS

THE Pan Indian Ocean Science Association was formed in January 1951, at Bangalore, India, when thirty-six delegates representing nine countries met for the first Pan Indian Ocean Science Congress. The 1951 meeting was mainly devoted to drafting a constitution for the Association, and in arranging working committees in each of the member countries. Much consideration was also given to the major scientific problems affecting these nations. This initial survey enabled the national committees during the 1951–54 inter-congress period to prepare many reports on problems of the Indian Ocean zone and on researches which had been carried out upon them. These reports provided material for the symposia and discussions of the second Pan Indian Ocean Science Congress, which was held in Perth, Western Australia, in August 1954 and attended by 527 people. Indonesia and Pakistan were admitted to membership of the Association at Perth; the other member countries are Australia, Burma, Ceylon, France, India, Madagascar, Malaya, the Netherlands and Portugal.

The Proceedings of the Congress, which appear in eight volumes, contain some of the original papers and an account of some of the discussion. The first volume contains the whole presidential address and also gives details of the constitution and membership of the Congress as well as recommendations by the whole Congress or by the separate sections of the physical sciences; biological sciences; geological sciences; agricultural sciences; economics, education, and social sciences; geography and oceanography and human ecology. The scientific papers of the various sections are set out in the remaining volumes.

The president at Perth was Prof. A. P. Elkin, professor of anthropology in the University of Sydney, who spoke about "The Natural History of Man".

The recommendations of the Congress give an indication of the wide-ranging scope of its deliberations and of the practical efforts made to secure co-operation in research and development for the whole area. Among the many important recommendations were the following.

Recognizing the importance of the preparation of detailed information on the distribution of plants and animals, particularly in coastal areas, the Congress recommended that co-operation be instituted with the Pacific Science Association in a similar project which the latter is undertaking, and that in future work more attention be devoted to the study of biocœnoses.

The Congress also recommended that continuous records of temperature, rainfall, humidity and sunshine for a range of type localities in each country be kept, and directed attention to the need for international agricultural quarantine regulations for the Indian Ocean region.

The Congress recommended collaboration in the preparation of climatic and other maps on a uniform basis, so that results obtained in any one country could be applied more systematically in other countries; collaboration in the collection of wild and cultivated forms of economic plants indigenous to the Indian Ocean region; collaboration in plant exploration in extra-regional areas of special significance for the Indian Ocean countries; and visits by and interchange of agricultural scientists of the Association countries with a special knowledge of plant introduction requirements and possibilities and thus able to stimulate useful exchanges of plant material.

Recognizing that the improvement of tropical grasslands offers great scope for improving the world's food supply and involves problems common to all Indian Ocean countries, the Congress recommended that information gained in these countries on this subject should be interchanged.

As mixed farming can play an important part in the development of tropical agriculture, the Congress recommended that there be concerted action in research on problems relating to this system of land use in the Pan Indian Ocean area.

The Congress suggested that the Association should undertake the preparation of a general handbook presenting in broad terms the present state of scientific knowledge of the Indian Ocean area as a whole; while Unesco was to be asked to assist in the development of facilities within existing stations of the area to train and interchange personnel.

The Unesco proposal to create a legally constituted inter-governmental organization for oceanographic research in the Indo-Pacific region was strongly supported.

Food problems were discussed, and the Congress recommended that exchange of information on the principles of food management should be organized; that a study of food habits and 'food fads' be made in the area; and that a study of elementary nutrition be included in primary education programmes. After considering tuberculosis and leprosy, the Congress recommended that an attack on socio-economic conditions, particularly housing, should be considered as the most effective factor in tuberculosis control and that primary education in living habits, with particular reference to spitting, and secondary education to produce trained personnel, should be emphasized in any tuberculosis-control programme; the institution of an effective method of prevention of leper migration to unaffected areas was recommended.

The secretary of the Congress is Prof. A. D. Ross, from whom at "Balnagown", Golf Links Road, Albany, Western Australia, copies of the full Proceedings may be obtained, price 37*s*. 6*d*. The next Congress is to be held at Tananarive, Madagascar, in September 1957.

METHODS FOR THE STUDY OF HUMAN RELATIONS IN INDUSTRY

DURING the War and the post-War period, in Western countries and more especially in the United States, there has been a gradual awareness of the need for a more adequate social-psychological approach to problems of human motivation and adjustment in industry. This approach is concerned with the satisfactions and motivations existing among the members of different groups in industries and how these can be improved by suitable changes in the groups and organizational structure. Psychology has contributed the maximum toward the development and refinement of techniques for study of human relations problems.

The psychologist, in his study of these problems, uses one or more of three distinct approaches. These are: (1) the attitude survey approach; (2) the group dynamics approach; and (3) the clinical psychology approach.

Each technique has its usefulness in its own field. The survey technique is particularly useful in the discovery of principles underlying problems of organizing and managing human activity. The Survey Research Centre of the Institute for Social Research at Ann Arbor is using it with advantage for the study of "social and interpersonal determinants of organizational effectiveness and employee satisfaction".

The group dynamics approach, developed on the conceptualizations of Kurt Lewin, is specially useful for the understanding of determinants of inter-group relations and of relations among members of a group. This approach, in combination with the sociometric technique, has made possible careful observation and analysis of group behaviour.

Psychotherapy is highly useful in specific cases; but its utility lies perhaps not in any improvement of human relations in industry by treating all those suffering from emotional maladjustments (there are not enough therapists for that even in the United States), but in analysing the effects of different types of personalities on the organizational structures set up by them, the top man's methods of dealing with people in the organization and the way it influences their attitude.

The ultimate object of various studies made along the above lines is to have an integrated theory of organized human effort which will be useful to society in general and to industry in particular. This can best be achieved by a close integration of ideas from different social sciences, psychology, sociology, economics, anthropology, etc. So far as human relations in industry are concerned, approaches are being made from different sides; substantial inter-professional collaboration is yet to be achieved.

Studies based on the above techniques and the changes based on findings from such studies that the psychologist attempts to introduce in the organizational structure carry some implicit value assumptions of what is desirable, what is good. As yet, little attempt has been made to make them explicit or justify them. Harish Chandra Ganguli suggests that this is all the more necessary for psychologists of countries other than the United States who try to use these techniques mostly developed in America and permeated with American values in a setting culturally and socially very much different from that of the country of origin (*Sci. and Cult.*, **21**, No. 12; June 1956).

PLANT GROWTH-REGULATING ACTIVITY IN CERTAIN CARBOXYLIC ACIDS NOT POSSESSING A RING STRUCTURE

By Dr. C. H. FAWCETT, Prof. R. L. WAIN and Dr. F. WIGHTMAN

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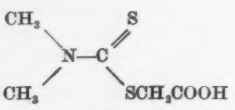
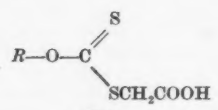
CHEMICAL structure in relation to plant growth-regulating activity of carboxylic acids has been the subject of much research over the past twenty years, and until recently it was considered that, in addition to the —COOH group, another essential requirement for activity was an unsaturated ring structure[1]. The discovery by van der Kerk and co-workers[2] that carboxymethyl dimethyldithiocarbamate (I) and certain of its analogues can show appreciable plant growth-regulating activity indicates that an unsaturated ring system may not be essential. These workers suggested, however, that the activity observed in these compounds is associated with the N—C bond acquiring double-bond character due to internal electron shifts, thus resulting in a type of 'ring' system[2]. This possibility has since been questioned[3].



(I)



(II)

We have synthesized a series of carboxymethyl O-alkyxanthates (II), and the tertiary butyl derivative ($R=(CH_3)_3C$—) was found to be significantly active in promoting the growth of 1-cm. wheat coleoptile sections (Table 1). The technique was exactly as described for the *Avena* cylinder test[4] except that wheat coleoptiles (var. Eclipse) were used. The fact that in the xanthates the O—C bond acquires comparatively little double-bond character[3] (as in the canonical form $R—O{=}C—S^-$) provides further evidence that a ring or partial ring is not essential for growth-regulating activity. Again, the small but significant activity reported by Bennet-Clark for dimethylacetothetin chloride[5] is consistent with the view that a ring system need not be present. The interesting possibility has been raised that the activity of the thetin is related to its known behaviour as a methyl donor[5]. Betaine hydrochloride, known to be less active in transmethylation, is inactive in the wheat test (Table 1).

In a study on the growth-promoting activity of chloro- and methyl-substituted acetic acids in the wheat coleoptile test, significant activity was found in a number of instances. Thus, for example, all three chloro-acids were active (Table 1), though no activity was shown by these or any other compounds of this group in the pea curvature test. The slight activity previously reported for trichloroacetic acid in the pea test[6] has not been observed in the present work.

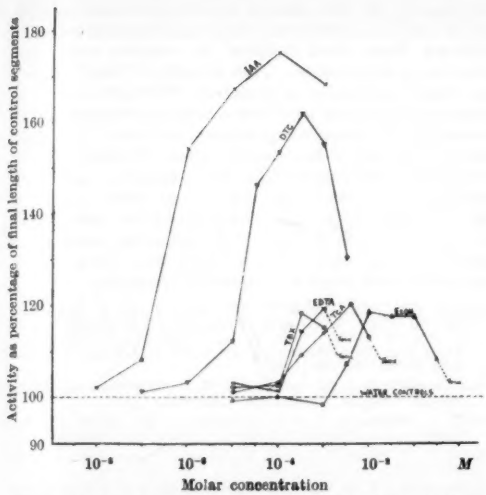


Fig. 1. Activity in the wheat cylinder test after 24 hr. of certain non-ring compounds relative to 3-indolylacetic acid. All acids tested as the sodium salts (EDTA as the tetra-salt). DTC, carboxymethyl dimethyldithiocarbamate; TBX, carboxymethyl O-*tert*-butylxanthate; EDTA, ethylenediaminetetraacetic acid; TCA, trichloroacetic acid; EtOH, ethyl alcohol

The first suggestion that chelating agents may show plant growth-regulating activity was made by Bennet-Clark at the Wye Symposium in 1955[5]. It was shown that ethylenediaminetetraacetic acid is capable of promoting slight extension growth both in oat and wheat coleoptile tissue, and this was attributed to a chelating mechanism whereby the calcium/pectin relationship in the cell wall was affected. The activity of ethylenediaminetetraacetic acid was independently observed by Heath and Clark[7], who also favour a chelation hypothesis. In support of this, they showed that whereas a number of other chelating agents possessed significant activity in the wheat cylinder test, various compounds not recognized as chelators possessed negligible activity. The suggestion was also made that highly active auxins such as 3-indolylacetic acid and 2 : 4-dichlorophenoxyacetic acid might owe their biological activity to chelating properties. In view of the limited capacity of these molecules to chelate with metals and their very high growth-regulating activity, this would appear unlikely. Furthermore, chelation cannot be a universal mechanism leading to all types of growth response, since in the pea curvature and tomato leaf epinasty tests, in which 3-indolylacetic acid and 2 : 4-dichlorophenoxyacetic acid are extremely active, ethylenediaminetetraacetic acid has been found to be completely inactive.

It is important that the activity of all these non-ring compounds should be seen in the right perspective. Heath and Clark[7] in one experiment with wheat coleoptile sections found ethylenediaminetetraacetic acid at 10^{-5} *M* gave practically the same increment of growth, compared with controls, as 3-indolylacetic acid at the same molar concentration. In a second experiment, the response to ethylenediaminetetraacetic acid was just significantly less than that shown by 3-indolylacetic acid. In the present work, using a different technique, ethylenediaminetetraacetic acid was found to be a much less active growth substance than 3-indolylacetic acid (Table 1, Fig. 1), a result previously found by Bennet-Clark using oat coleoptile segments[5].

It therefore became necessary to carry out further experiments in which the activities of ethylenediaminetetraacetic acid and 3-indolylacetic acid were compared after treatment periods of 24, 36 and 48 hr. The analytically pure compounds were tested both as the free acids and as their sodium salts, all four salts being included in the case of ethylenediaminetetraacetic acid. The results for the salts were similar to those obtained with the acids and, furthermore, no significant differences were observed

Table 1. The Activity of certain Carboxylic Acids in the Wheat Cylinder Elongation Test*

Formula of compound	Concentration in p.p.m. 0·1	1	10	100	500	1,000
CH_3COOH	100	104	101	102	100	99
CCl_3COOH	100	101	107	**117**	**125**	**119**
$C(CH_3)_3COOH$	101	102	102	102	104	101
$CHCl_2COOH$	99	100	**109**	**110**	**122**	**117**
$CH(CH_3)_2COOH$	103	102	106	105	105	100
$CH_2ClCOOH$	99	102	103	**112**	Toxic	Toxic
CH_3CH_2COOH	100	103	102	100	97	93
$CH_3CHClCOOH$	100	102	107	**116**	104	96
CH_3CCl_2COOH	99	102	102	**109**	106	100
$(CH_3)_2CClCOOH$	101	102	101	98	98	96
$CH_3OCSSCH_2COOH$	98	102	98	101	93	92
$C_2H_5OCSSCH_2COOH$	103	98	98	98	93	Toxic
$(CH_3)_2CHOCSSCH_2COOH$	100	98	96	94	Toxic	Toxic
$(CH_3)_2COCSSCH_2COOH$	102	100	103	**114**	Toxic	Toxic
$(CH_3)_2\overset{(+)}{S}(Cl)\overset{(-)}{C}H_2COOH$	100	104	102	**115**	Toxic	Toxic
$(CH_3)_2\overset{(+)}{N}(Cl)\overset{(-)}{C}H_2COOH$	100	97	105	93	Toxic	Toxic
$(CH_3)_2NCSSCH_2COOH$	101	98	**120**	**162**	**138**	**129**
$(C_2H_5)_2NCSSCH_2COOH$	98	100	**118**	**137**	**122**	**114**
$(CH_3)_2NCOSCH_2COOH$	96	98	99	103	**134**	**126**
$(CH_3)_2NCSOCH_2COOH$	**131**	**150**	**148**	**154**	**139**	**132**
$(CH_3)_2NCSSC(CH_3)_2COOH$	101	99	98	102	99	100
$(HOOCCH_2)_2N.CH_2CH_2.N(CH_2COOH)_2$†	98	99	101	110	118	Toxic
3-Indolylacetic acid	**143**	**165**	**158**	**156**	—	—
2 : 4-Dichlorophenoxyacetic acid	**125**	**154**	**160**	**132**	—	—

Figures in heavy type are significantly different from controls at the 0·1 per cent level

* All compounds were examined at stated concentration of the acid in the form of its sodium salt. Responses were measured after 24 hr. and activity expressed as percentage of final length of control segments.

† Tetra-sodium salt.

in the results obtained for the various treatment periods. It is apparent from Fig. 1 that ethylenediaminetetraacetic acid is very much less active for promoting extension growth in wheat coleoptiles than is 3-indolylacetic acid. Indeed, in these experiments ethylenediaminetetraacetic acid showed the same low order of activity as trichloroacetic acid and carboxymethyl O-*tert*-butylxanthate (Fig. 1). In view of the fact that these three non-ring compounds are completely inactive in the pea curvature test and that their capacity to induce slight growth responses in wheat coleoptile tissue is only revealed at near-toxic concentrations, it is possible that the compounds are not acting as true 'growth substances'. In agreement with this, the shape of the growth/time curves at optimum concentrations indicates that the pattern of growth is not typical of a normal auxin response. The action of these substances may well depend upon changes in membrane permeability and cell wall structure resulting from sub-acute toxicity.

To examine this possibility further, a study was made of the behaviour of ethyl alcohol in the wheat test. This compound showed the same low order of growth response (Fig. 1), and, furthermore, the highest activity was revealed at a concentration just below the level at which toxic symptoms were observed. Moreover, the type of elongation observed was typical of that shown by ethylenediaminetetraacetic acid, trichloroacetic acid and the xanthate and different from that induced by sugars and other respiratory substrates. This activity of ethyl alcohol has been confirmed a number of times, and it is suggested that this provides a further example of the 'non-typical' growth-regulating activity discussed above. On the other hand, certain dimethyldithiocarbamate derivatives (I), for example, can show appreciable activity in the wheat test (Table 1, Fig. 1), and since such compounds are also active in the pea and tomato-leaf epinasty tests it is probable that this type of non-ring structure is capable of inducing a true auxin response.

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INHIBITION OF PLANT CYTOCHROME OXIDASE BY BICARBONATE

By GENE W. MILLER and Prof. HAROLD J. EVANS

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THE concentration of carbon dioxide in equilibrium with bicarbonate in the soil has been recognized as an important ecological factor for many years[1]. Recent experiments by Thorne *et al.*[2] have indicated that the level of bicarbonate in nutrient media is positively correlated with the incidence of lime-induced chlorosis. Bean plants grown in nutrient cultures in which *p*H and bicarbonate concentrations were varied by controlling the carbon dioxide pressure of the aeration stream developed chlorosis at the high bicarbonate levels regardless of the *p*H of the solutions. Further experiments[3] indicated that the inhibition by bicarbonate of the respiratory rates of roots from chlorosis-susceptible species was greater than that of the roots from chlorosis-resistant species. A study[3] of the carbon monoxide inhibition of oxygen uptake provided indirect evidence that cytochrome oxidase was the dominant terminal oxidase in the bicarbonate-susceptible plants, and possibly was the factor affected by bicarbonate salts.

The experiments reported herein provide direct evidence that bicarbonate is an inhibitor of cytochrome oxidase from certain higher plant species. These experiments were conducted in conjunction with a more detailed study of the stimulatory effects of various salts on cytochrome oxidase activity.

In the experiment illustrated in Fig. 1 the effect of sodium bicarbonate on the activity of cytochrome oxidase from two species was compared with that of sodium chloride on the activity of the enzyme. Particulate preparations containing cytochrome oxidase were made from the roots of spinach (*Spinacia*

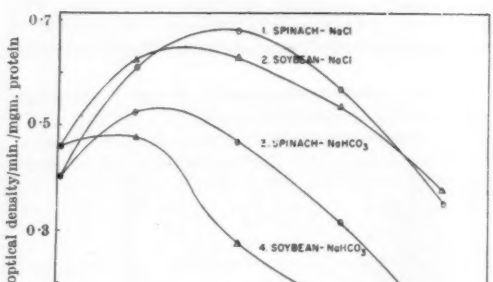

Fig. 1. The effect of sodium bicarbonate compared to sodium chloride on cytochrome oxidase activity of soybean and spinach roots. The complete system (curve 1) contained 50 μmoles tris buffer at *p*H of 8·8, 0·051 μmole reduced cytochrome *c*, extract of particulate material from spinach roots and concentrations of sodium chloride indicated in a final volume of 1 ml. Curve 2, identical reaction mixture with the exception that the extract was obtained from soybean roots. Curve 3, the assay mixture was identical to that for curve 1 with the exception that sodium bicarbonate was added instead of sodium chloride. Curve 4, the reaction mixture was identical with that for curve 2 with the exception that sodium bicarbonate replaced sodium chloride. Reactions were started by addition of extract containing 0·1–0·2 mgm. protein, and stirred prior to each reading to avoid errors due to the settling of particles in the cuvette

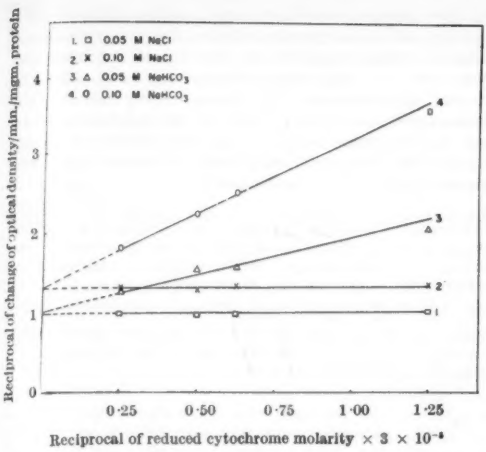

Fig. 2. Lineweaver–Burk plot of the inhibition of cytochrome oxidase activity of soybean roots by sodium bicarbonate. Assay mixtures in a final volume of 1 ml. contained 50 μmoles tris buffer at *p*H 8·8, desired concentration of reduced cytochrome *c*, the indicated type and concentration of salt and extract containing 0·12 mgm. protein. Readings were taken every 10 sec. and enzyme activity calculated as the change in optical density per min. per mgm. protein using only the linear portion of optical density change per unit of time

oleracea L., variety Bloomsdale) or soybean (*Glycine max* Merr., variety Ogden) plants 6–30 days old as previously described[4], with the exception that the isolation medium contained 0·05 *M* tris-hydroxymethyl-aminomethane buffer at *p*H 7·5 instead of phosphate buffer. Reduced cytochrome *c* was prepared chemically by the use of sodium hydrosulphite[4] and the assays were determined spectrophotometrically at 550μ with a Beckman *DU* spectrophotometer[4]. The enzyme activity is indicated as the decrease in optical density between 15 and 75 sec. after the reaction was started by the addition of enzyme. Under the conditions of the experiments, the oxidation rates were linear for two minutes after the reactions had begun. The protein content of the extracts was determined by the use of Folin's phenol reagent[5].

The curves in Fig. 1 show that cytochrome oxidase from the roots of both spinach and soybean plants is stimulated by concentrations of sodium chloride up to 0·1 *N*; but concentrations greater than this resulted in decreases in activity. The influence of variable concentrations of sodium nitrate and sodium sulphate was practically identical to that of sodium chloride. It is apparent from Fig. 1 that various concentrations of bicarbonate at *p*H values comparable to those where chloride salts were used inhibited cytochrome oxidase activity from 20 to 75 per cent, depending on the bicarbonate concentration. This inhibitory effect also has been observed with cytochrome oxidase preparations from oat and tobacco plants and from pig heart. The inhibitory action of bicarbonate has been observed in assay mixtures adjusted to *p*H 7·8 by use of tris-hydroxy-aminomethane buffer and carbon dioxide. The inhibition is not limited, therefore, to the high *p*H conditions used in the experiment shown in Fig. 1.

The influence of sodium bicarbonate on cytochrome oxidase activity of soybean root extracts at various reduced cytochrome *c* concentrations was determined, and the reciprocals of enzyme activities plotted against the reciprocals of reduced cytochrome *c* concentrations according to the method of Lineweaver and Burk[6] (Fig. 2). The results from assays containing concentrations of 0·05 *M* (curve 3) and 0·10 *M* (curve 4) sodium bicarbonate were compared with those from assays containing equivalent amounts of sodium chloride (curves 1 and 2). These results indicate that sodium bicarbonate is a competitive inhibitor of cytochrome oxidase.

Since it was apparent that bicarbonate inhibited cytochrome oxidase *in vitro* and since evidence in the literature indicated that excessive bicarbonate in culture media is detrimental to plant growth and is associated with chlorosis of leaves, it was deemed necessary to determine whether the addition of bicarbonate to culture solutions would influence the activity of cytochrome oxidase in tissues. To test this possibility, soybean plants of the Ogden variety were grown in pots of washed quartz sand in the greenhouse. Seven seven-day-old seedlings were transferred to each of twelve polyethylene pots of quartz sand. The pots held a volume of 6 litres and each was equipped with a drain hole in the bottom. Four treatments replicated three times were applied to the cultures in a randomized block experiment. The treatments indicated in Table 1 consisted of 0·008 *M* and 0·016 *M* sodium bicarbonate and 0·008 *M* and 0·016 *M* sodium chloride + sodium hydroxide. The variable culture treatments were added to a standard Hoagland nutrient solution, and the soybean cultures were flushed with the appropriate solutions three times daily. The *p*H of the effluent from cultures receiving sodium chloride + sodium hydroxide ranged between 7·5 and 7·7 and that of the effluent from cultures receiving sodium bicarbonate ranged between 7·6 and 7·9. After 25 days the plant receiving bicarbonate in solutions developed a chlorosis of leaves. At that time roots were harvested and extracts prepared from them by the method indicated in the experiment reported in Fig. 1. Results of assays presented in Table 1 show that the extracts from plants receiving the bicarbonate treatments were significantly lower in cytochrome oxidase activity than extracts from plants grown with comparable concentration of sodium added as the chloride and hydroxide. The inhibitory effect of the 0·008 *M* sodium bicarbonate treatment on the enzyme activity was significant at the 1 per cent level and the effect of the 0·016 *M* sodium bicarbonate

Table 1. The Effect of Sodium Bicarbonate in Culture Solutions on the Cytochrome Oxidase Activity of Extracts from Roots of Soybean Plants

Culture treatment		*p*H of culture solution	Cytochrome oxidase activity†	Appearance of chlorosis
NaCl+NaOH*	$NaHCO_3$			
M	*M*			
0·008	0·000	7·7	1·13	−
0·000	0·008	7·7	0·67	+
0·016	0·000	7·8	0·92	−
0·000	0·016	7·8	0·60	+
L.S.D. (1 per cent			0·34	
L.S.D. (5 per cent)			0·23	

* Treatments containing no sodium bicarbonate were adjusted to the desired *p*H with sodium hydroxide, and sufficient sodium chloride was added to give a concentration of sodium comparable to the bicarbonate treatments.

† The reaction mixture in a final volume of 1 ml. contained 50 μmoles tris buffer at *p*H 7·5, 0·051 μmole reduced cytochrome *c* and extract prepared from roots of soybean plants grown with the various treatments and containing from 0·08 to 0·09 mgm. protein. Results are means of duplicate determinations from three replicate cultures and are expressed as optical density change at 550 mμ per minute per mgm. protein.

treatment approached this level of significance. As indicated in Table 1, the plants supplied with sodium bicarbonate developed a chlorosis of leaves; but this symptom was not apparent with plants grown without bicarbonate. There was no influence of treatment on the total growth of plants. Other treatments not reported indicated that extracts from plants grown with culture solutions with various *p*H values were not significantly different in cytochrome oxidase activity.

From the above results it seems clear that excessive concentrations either *in vitro* or *in vivo* inhibit cytochrome oxidase activity. Since the inhibition is competitive in respect to reduced cytochrome *c*, the inhibition in living tissues containing relatively low concentrations of cytochromes may be considerably greater than that indicated from assays conducted with relatively high cytochrome *c* concentrations. Further experimentation may prove that the inhibition of cytochrome oxidase by bicarbonate is related to the inhibition by this ion of respiration of plant tissues[3]. Also, these results may have a bearing on the observations that bicarbonate induces the accumulation of organic acids in excised barley roots[7] and on the observation that the tissues of plants affected by lime-induced chlorosis contain excessive concentrations of organic acids[8].

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A CYTOLOGICAL STUDY OF THE NEURONES OF *PATELLA VULGATA* BY LIGHT AND ELECTRON MICROSCOPY

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AND

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IN view of various conflicting reports on the cytology of neurones of Mollusca[1-5] a study has been made of neurones from the pedal, pleural and visceral ganglia of the common limpet *Patella vulgata* by both light and electron microscopy.

Observations by Light Microscopy

When cells were treated by Kolatchev's method for the Golgi apparatus (post-osmification for 24 hr.) two types of inclusions were revealed: lipochondria (lipochrome granules, neutral-red bodies) and Golgi apparatus. The lipochondria were spheroidal in form, ranged in colour from light to dark brown, and varied greatly in number in different neurones. In large cells they typically clustered around a well-defined, and approximately central, region which, from evidence presented mainly by electron microscopy, was identified as an active secretory zone and will be termed the *S* region (Fig. 1). The Golgi apparatus nearly always appeared as a network of fine strands and only occasionally as apparently discrete curved dictyosomes. Both networks and dictyosomes were black in colour. Associated with some of the networks and dictyosomes was a weakly osmiophilic, diffuse material identified as archoplasm. In large neurones the Golgi apparatus ramified the *S* region and was therefore generally distinct topographically from the lipochondria. In small neurones the Golgi apparatus occupied a small juxta-nuclear region. The latter probably corresponds to the *S* region of larger cells.

It is generally accepted that iron haemotoxylin and acid fuchsin will stain mitochondria after appropriate fixation. Bleached Kolatchev preparations were stained, therefore, with iron haemotoxylin, and Helly post-chromed sections with acid fuchsin. The iron haemotoxylin stained small granules and rods which varied considerably in number from cell to cell and which were generally situated towards the periphery of the *S* region and among the lipochondria. By a study of individual cells both before bleaching

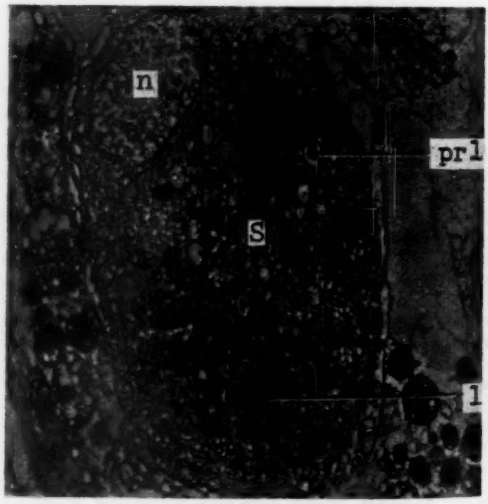

Fig. 1. Low-power micrograph showing the '*S*' region. Several pro-lipochondria (*prl*) and lipochondria (*l*) can also be seen. n = nucleus. (× 6,000)

and after staining with iron haemotoxylin, it was established that the Golgi apparatus is definitely not an artefact caused by the over-impregnation of mitochondria as maintained by Thomas[5].

In Helly preparations the acid fuchsin stained small granules and rods (similar to those revealed by iron haemotoxylin) and, to a less extent, the lipochondria. Some of the small granules were larger than others. Both in this respect and in their staining reaction they seemed to represent a stage in the formation of the lipochondria. Thus the acid fuchsin was apparently staining mitochondria, developing lipochondria, and mature lipochondria. (It is probable that the iron haemotoxylin also stained the mitochondria and developing lipochondria.) In cells containing many small fuchsinophil granules there were few lipochondria and vice versa.

Within the limits of resolution of the light microscope, the cell body of these neurones extended into a single nerve process. The position of the nucleus relative to the process was very variable. Often it lay either near the process or, on the other hand, at the extreme opposite end of the cell body. Rarely did we see a nucleus in the central position as so often depicted for cells of this kind[1-7]. Each nerve process passed from the outer (cortical) region of each ganglia into the central (medullary) part, where it met numerous other nerve fibres.

Each nucleus usually contained a single prominent nucleolus which was intensely osmiophilic and stained strongly with iron hæmotoxylin, acid fuchsin, and methylene blue. When Champy post-chromed preparations (gelatine embedded) were stained with acid fuchsin a few minute granules were seen in the nucleoplasm in addition to the nucleolus.

Kolatchev preparations not only revealed the lipochondria and Golgi apparatus but also fine fibrils within the nerve fibres.

Observations by Electron Microscopy

Studies on neurones treated by Kolatchev's method, or on those fixed in buffered osmium tetroxide and examined at high resolution with a Siemens Elmiskop I, substantiated and extended the observations recorded above. The following account refers to material fixed in buffered osmium tetroxide except when stated otherwise.

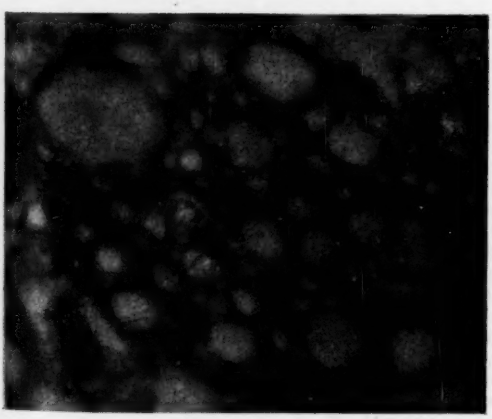

Fig. 2. Micrograph showing the ultrastructure of a lipochondrion. The internal network of membranes divides the inclusion into a number of osmiophobic compartments. (× 40,000)

Fig. 3. Micrograph showing paired Golgi membranes. (× 120,000)

The lipochondria, which generally appeared homogeneous in light microscopical preparations, were either homogeneous or consisted of an elaborate internal network of membranes (Fig. 2). The Golgi apparatus had essentially the same ultra structure as in many kinds of vertebrate cells[8,10]. It consisted of paired anastomosing membranes which usually enclosed an inner dense (osmiophilic) substance, a vacuolar (osmiophobic) material lying within dilations of the paired membranes, discrete vacuoles, and small vesicles (Fig. 3). The networks and dictyosomes seen in light microscope preparations were due to the impregnation of the paired membranes and inner substance; the archoplasm probably resulted from the impregnation of the Golgi vesicles. The mitochondria were generally few in number and were either rod-like with numerous cristae[11] or spheroidal with few cristae (see below).

The *S* region was seen with great clarity (Fig. 1). Within this region was the Golgi apparatus, occasional rod-like mitochondria, and numerous spheroidal bodies. The last-named were generally smallest in the centre of the *S* region and largest towards its periphery, where they lay among the lipochondria. Some of the spheroids were identified as mitochondria although the limiting membrane was not always completely double. Cristae were few and small, and the matrix was osmiophobic. The majority of the spheroids possessed only a single external 'limiting' membrane, an internal coiled membrane, and an inner substance containing various amounts of a very dense (osmiophilic) material. The appearance of the last-named inclusions strongly suggested that they represented stages in the formation of the osmiophilic lipochondria. Provisionally they will be referred to as *pro-lipochondria* (Fig. 1). The evidence both from light microscopy (*vide* results with acid fuchsin above) and electron microscopy suggested that the pro-lipochondria were of mitochondrial origin. It may be emphasized here that lying between all the spheroids (mitochondria and pro-lipochondria) were masses of Golgi vesicles. This may suggest that the Golgi apparatus plays some part in the formation of the lipochondria.

Another kind of cell inclusion, lying below the limits of resolution of light microscopy, was revealed by the electron microscope. This inclusion consisted of a small vacuole with a dense granule embedded in its periphery. Such structures were observed generally towards the periphery of the cell body, although some were seen also in the *S* region.

The cells did not contain a highly developed system of ergastoplasmic membranes[12]. Typically they

bordered lamelliform or large vesicular masses of ergastoplasm. Occasionally the membranes formed conspicuous whorl-like figures similar to those described by Palay and Palade[13] in vertebrate neurones. Some cytoplasmic particles[14] were in contact with one side of the ergastoplasmic membranes except when the latter were whorl-like in form. Numerous such particles lay free in the cytoplasmic matrix.

Each neurone was bounded by a single membrane. Frequently it appeared as if two membranes were present. However, in such cases the outer membrane belonged either to an adjacent cell body or nerve fibre. Each nerve fibre contained a variable number of neurofibrils (individually below the limits of resolution of the light microscope) and small mitochondria. In Kolatchev preparations studied by electron microscopy the osmium either was deposited heavily on single neurofibrils or, more usually, between them. In either way this accounted for the appearance under the light microscope of fine fibrils in nerve fibres treated by Kolatchev's technique. In material fixed in buffered osmium tetroxide, tangled masses of neurofibrils were observed passing around vacuolated bodies and small vesicles. It is possible that the vacuolated bodies and vesicles may serve as the nidus for the formation of the neurofibrils.

Both the lipochondria and the vacuole-granule inclusions described above were observed in nerve fibres. It appears, therefore, that each is a definite secretory product of the neurones. It is of particular interest that lipochondria appear to be formed in essentially the same way as are zymogen granules in exocrine cells of the pancreas[15,16]. Thus a common method of synthesizing secretion products apparently exists in such diverse types of cells as the neurones of a gastropod and pancreas cells of mammals.

We wish to express our appreciation to Drs. A. J. Marshall and V. E. Cosslett for their interest and encouragement in this work and to Mr. G. Rogers for his help in the cutting of ultra-thin sections. One of us (R. H.) is indebted to the Agricultural Research Council for financial support.

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ROLE OF OXYGEN IN MODIFYING THE RADIOSENSITIVITY OF *E. COLI* B.

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IN the course of X-ray experiments on *E. coli* B., it was found that the radiosensitivity of the bacteria was increased by oxygen concentrations as low as 1 μmole/l. This is very small compared with the concentration required to effect a similar change in other materials used in radiobiological experiments[1,2]. Oxygen concentration is measurable only in the fluids surrounding the cells or tissues concerned, and the assumption that it is the same within the cells seems best justified for micro-organisms, singly dispersed in a medium supplied with oxygen at a rate far exceeding that required for respiration. The effect of varying the oxygen concentration on the radiosensitivity of *E. coli* B. has therefore been investigated by irradiating very dilute suspensions while the required gas mixture was passed through the suspending medium in a vigorous stream of fine bubbles.

The bacteria were in the stationary phase, harvested 16–20 hr. after inoculation, from unaerated nutrient broth which then contained about 2×10^9 organisms/ml. The suspensions for irradiation were prepared by centrifuging the cultures, washing three times and resuspending in buffered saline (sodium chloride 0·13 *M*, phosphate buffer 0·02 *M*, *p*H 7·0); aliquots were then used for making up suspensions in buffered saline at the dilutions required. Irradiations were carried out at 20° C. with 200 kV. X-rays filtered by 2 mm. aluminium, at 2,000 rads/minute. 'Survivors' in the bacterial population were defined as those bacteria which retained the ability to form macrocolonies on nutrient agar plates incubated at 37° C. Survival curves were found to be exponential in all experiments. The radiosensitivity was defined as the slope of the line relating the logarithms of survivors to the dose. The radiosensitivity was found to be independent of the concentration of bacteria between 6×10^8 and 2×10^9 organisms/ml. and also independent of the respiration-rate. It appeared to depend only on the oxygen concentration at the time of irradiation. The survival curves were identical for bacteria which were held anaerobically from the time of harvesting until irradiation commenced, and for those which, in dilute substrate-free suspension, had been exhausted by oxygen bubbling at 30° C. for 1½ hr. Moreover, radiosensitivity was the same for suspensions which were free from substrate and those which contained potassium succinate at 0·01 *M*. The effect of the succinate on respiration-rate was demonstrated by measurements on a dense washed suspension of *E. coli* B. The rate of oxygen uptake was increased by a factor of 5 when succinate was added after 40 min. of endogenous respiration (we are indebted to Dr. F. A. Holton for making this measurement).

The relationship between radiosensitivity and oxygen concentration was determined by establishing

survival curves under nitrogen, oxygen and a range of nitrogen – oxygen mixtures. A typical set of survival curves is shown in Fig. 1. The variation of radiosensitivity with oxygen concentration is shown in Fig. 2. The solid line (curve A) represents the equation

$$\frac{S}{S_N} = \frac{m[O_2]+K}{[O_2]+K} \qquad (1)$$

where S_N is radiosensitivity in the absence of oxygen; $[O_2]$ is oxygen concentration in micromoles of oxygen per litre; S is radiosensitivity at an oxygen concentration $[O_2]$; m and K are constants, respectively 2·9 and 7·2 micromoles/litre for curve A.

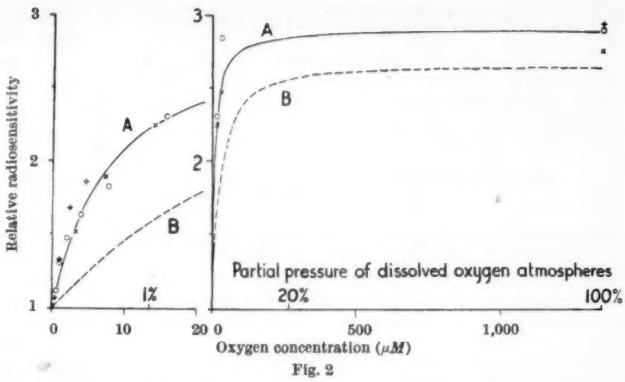

Fig. 2

The relationship between radiosensitivity and oxygen tension in other materials could also be described by an equation of the form given. In many cases the value of the constant m is close to 3 [1,2]. The value of K obtained for *E. coli* B. is, however, considerably lower than that obtained by fitting equation (1) to various sets of data in the literature: for example, Conger's data[2] on ascites tumour cells are fitted by $m = 3·6$, $K = 135$ μmoles/l. It remains to be determined whether K does in fact vary over a wide range, depending on the material and the test of damage, or whether the low value obtained in these experiments reflects the fact that oxygen pressure in the cells is more nearly the same as that measured than has been the case in the conditions of other experiments.

A relationship of the type expressed by equation (1) can be derived from various mechanisms which might be postulated to account for the oxygen effect.

HO_2 radical hypothesis. It has frequently been suggested that primary damage to biological targets may occur by a mechanism analogous with that which increases the yield of oxidation products in aqueous solutions irradiated in the presence of oxygen. This mechanism is believed to be the conversion of hydrogen to HO_2 radicals if oxygen is present. The oxidation of ferrous ions in 0·8 N sulphuric acid has been investigated by Ebert[3]. Equation (1) fits his data well with $m = 2·7$, $K = 22·4$ μmoles/l., and curve B of Fig. 2 represents the equation with these constants. In the chemical system, it can be presumed that there is far less competition for hydrogen radicals than in the living cell, where there must be a great number of competing molecules. For example, Alper (unpublished work) has found that herring sperm deoxyribonucleic acid in aqueous solution is an extremely efficient scavenger of hydrogen radicals. It is to be expected that, to bring about a given change in radiosensitivity by means of HO_2 radicals, a higher oxygen concentration is needed in the presence of a radical-acceptor. If the mechanism for the oxygen effect is the same, the constant K of equation (1) should be higher, or at least not lower, in the living cell than in solutions free from organic solutes. As the opposite was observed, it appears to us unlikely that the enhancing effect of oxygen can be accounted for by HO_2 radicals effecting primary damage.

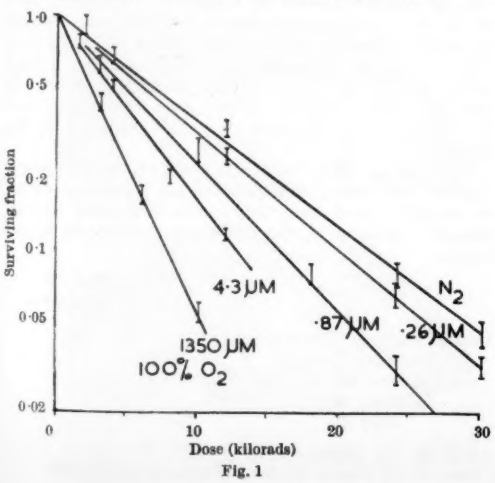

Fig. 1

Respiratory enzyme hypothesis. It is unlikely that radiosensitivity depends upon the state of the respiratory enzymes[3], as Longmuir[4] has shown that *E. coli* respire at half their full rate at an oxygen concentration of 2×10^{-6} M, whereas we found that more than 300 times as much oxygen was required to reach half the maximum radiosensitivity in *E. coli* B.

Direct effect hypothesis. In searching for an explanation of our observations on the oxygen effect on *E. coli* B., we have been led to postulate that the primary action of radiation in preventing cell multiplication is to ionize a vital target structure or molecule, which is then left in a highly reactive state, so that it will be involved in a chemical reaction within a very short time, probably less than a millisecond. The subsequent fate of the target molecule will depend on the nature of this reaction, which will affect the likelihood of its restoration to a functional state. If oxygen is present during irradiation, it will react with the ionized target and very much reduce the probability of restoration, so that a greater degree of damage will be apparent; but if it is admitted to the cell within a short time after the passage of the ionizing particle, it will be too late to take part in the reaction.

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LETTERS TO THE EDITORS

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Output of Sympathin from the Spleen

Qualitative studies of the nature of 'sympathin', the vasopressor substance appearing in the venous blood after stimulating post-ganglionic adrenergic nerves, have shown that it consists of a mixture of adrenaline and noradrenaline. We have recently been investigating quantitative aspects of sympathin output from the spleen with particular attention to the effect of the frequency of stimulation.

The method used was to stimulate the splenic nerves of the chloralosed cat and to measure the sympathin, assayed as noradrenaline, appearing in the venous blood. Peart[1] and Mann and West[2] have shown that sympathin from the spleen is almost entirely noradrenaline. The spleen was isolated from the stomach, pancreas and omentum, but retained its own circulation. The venous blood from the organ could be temporarily diverted to a polythene cannula in the superior mesenteric vein by occluding the portal vein. The blood from the cannula was collected in chilled, silicone-coated centrifuge tubes containing solid heparin. These precautions prevented the formation of masking substances. The volume of the separated plasma was measured and its 'sympathin' content assayed on the pithed rat's B.P. The splenic nerves were stimulated with rectangular pulses known to be supramaximal. Since we were interested in the effect of the frequency of stimulation on the output, the total number of stimuli was kept constant at 200 stimuli irrespective of the frequency. Both adrenal glands were removed and both major splanchnic nerves cut.

The output of sympathin, expressed as output/stimulus, showed a remarkable variation with the frequency of stimulation. This is summarized in Fig. 1. At low frequencies, little sympathin appears in the venous blood; but the output rises sharply as the frequency increases, to reach a maximum at about 30 pulses per sec. In constructing this graph allowance must be made for variations in the plasma flow in the period of collection. The output of sympathin varies with flow, and if this is reduced the output falls. The figures used in this graph lie in the same range of plasma flow.

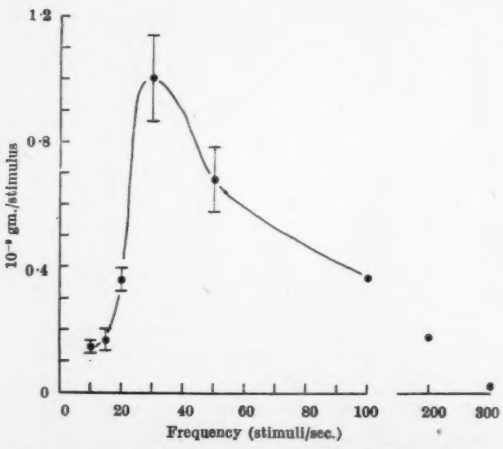

Fig. 1. Mean output/stimulus of 'sympathin' plotted against the frequency of stimulation. At all frequencies of stimulation the total number of pulses was 200. The vertical lines represent the standard errors of the means. Figures for 100, 200 and 300 pulses per sec. are single observations

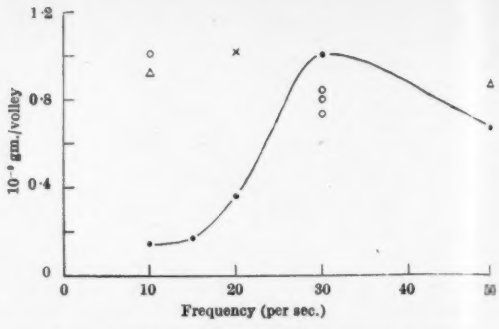

Fig. 2. First part of the graph in Fig. 1 with an extended scale for frequency. The individual results from three animals previously given 'Dibenamine' are shown. The output/stimulus at 10 pulses per sec. has increased and equals the maximum in the untreated animal. There is no obvious variation with frequency

Several explanations of this variation with frequency were possible. It might be that the more prolonged exposure to amine oxidase of the sympathin liberated at lower frequencies permitted a greater destruction of the active amine. This was tested by inhibiting the amine oxidase with isopropyl isonicotinyl hydrazine ('Marsilid'). The output before and after 'Marsilid' was the same.

Another possibility was that although the amount of sympathin released by each nerve volley was constant, the amount utilized by the tissue receptors was greater when the rate of release was slowed, that is, at low frequencies of stimulation. This was tested by blocking the tissue receptors with N.N. dibenzyl-β-chloroethylamine ('Dibenamine') and measuring the output/stimulus at varying frequencies. The results are shown in Fig. 2.

The first part of the previous graph has been drawn with an extended scale for frequency. Superimposed on it are the individual results for three experiments in which 'Dibenamine' had been given to the animal. The output at 10 pulses per sec. is increased some sevenfold and now equals the maximum output in the untreated animal. Furthermore the difference in output with frequency in this range has disappeared.

We suggest that the explanation of these observations is that the sympathin release per nerve volley is constant, and that the fraction utilized by the tissues is greater at the lower frequencies of stimulation.

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Autoradiography of End-plates with Carbon-14 – Calabash – Curarine I and Carbon-14 – Decamethonium

A HUNDRED years have passed since Claude Bernard's publication of his investigations on the action of curarine in "Leçons sur les effets des substances toxiques et médicamenteuses"[1]. He was able by indirect experiments to localize the curare-block in the end-plates of skeletal muscle. Some time ago when we investigated the metabolism of carbon-14 – curarine I in the cat[2], we tried to obtain autoradiographs of muscle, intending to show the fixation of this alkaloid directly at the neuro-muscular junctions.

For this purpose we had to synthesize carbon-14 – curarine of the highest possible radioactivity by methylation of 2·0 mgm. nor-curarine with an excess of 6·4 mgm. $^{14}CH_3I$, having the activity of 1 mc. After recrystallization we obtained 0·25 mgm. pure carbon-14 – curarine – iodide (biquaternary) with an activity of 24·2 μc./mgm. The minimal lethal dose of the water solution was injected into the veins of the tails of mice, which died of asphyxia within 40–120 sec. The diaphragms of these animals were stretched over steel rings of the same diameter (22 mm.) and dried in air. They were then brought into contact with X-ray film (Ilford X-ray PM_1) or mounted on microscope slides and covered by stripping film (Kodak). After developing the films the end-plates were stained by the Koelle method, in which acetylthiocholine is split by the cholinesterase, brown copper sulphide finally resulting[3].

After 60 days the resulting pictures on X-ray film showed a slight blackening in the region of the end-plates, which lie in a band of 260μ thickness around the centrum tendineum. In addition, there was blackening over the centrally situated vessels due to radioactivity in the blood. On microscopic examination of the stripping film a diffuse formation of silver grains over the end-plates was seen; but the crossfire over this region had been so heavy that only twice the grain density existed over each end-plate as compared to its immediate surroundings. The whole region had a 4–6 times higher density of grains compared with a corresponding region of muscle without end-plates.

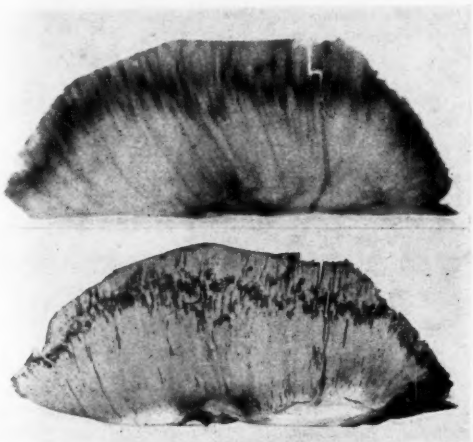

Fig. 1. Autoradiography of mouse diaphragm with carbon-14–decamethonium in comparison with staining of end-plates in the same diaphragm by the Koelle method (× c. 4)

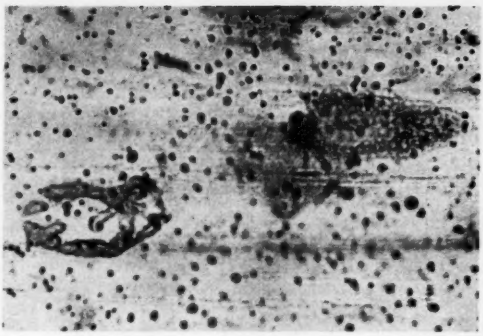

Fig. 2. Stained end-plates (Koelle method, × c. 700) and silver grains in stripping film by carbon-14–decamethonium

In order to obtain a much higher specific activity in a curarizing molecule we then methylated decamethylendiamine with $^{14}CH_3I$ and obtained 0·44 mgm. decamethonium with six carbon-14 atoms. The specific radioactivity was approximately five times larger than that of carbon-14 – curarine. After five days the resulting autoradiographs again showed clearly the localization over the end-plates, especially when compared with the stained diaphragms (Fig. 1). Over this region we counted four times more silver grains in the unit area of stripping film than in the muscle layer farther out (Fig. 2).

These pictures thus prove the fixation of 'curarizing' and 'depolarizing' drugs in the end-plate. They make possible the calculation of the number of molecules reacting with the receptor surface. We found 8×10^6 curarine molecules bound to one end-plate and $1{\cdot}7 \times 10^{12}$ molecules/cm.^{2} of apparent area of end-plate membrane, thus neglecting the possibility of a large increase in surface due to the palisade structure described by Couteaux[4]. The order of magnitude of apparent coverage of the end-plate surface is 5 per cent.

Details will be published in *Archives internationales de Pharmacodynamie et de Thérapie*.

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Globulins in the Chicken Egg-White

LONGSWORTH *et al.*[1] demonstrated, by electrophoresis in the Tiselius apparatus, three globulins in the white of an egg. These were labelled G_1, G_2, G_3. (G_1 was identified later with the lysozyme.)

The antigenic properties of egg-globulins were demonstrated first by Hektoen and Cole[2] and later by me[3].

In my studies on egg-white and its constituents[3–5], I have employed the methods which permit the analysis of complex mixtures, such as electrophoresis

and immunochemical techniques in agar gel. Thus, for the demonstration and enumeration of egg-globulins, four methods were used: (1) zone electrophoresis on paper and in agar gel[6]; immunological techniques (in this communication we give only the qualitative ones); (2) specific precipitation by double diffusion in agar plates[2-5] and (3) immunoelectrophoresis[7]; and (4) ultracentrifugation.

In this work, I have always studied comparatively the entire egg-white and its fractions, prepared chiefly by salting out with ammonium sulphate between 25 and 50 per cent of saturation. These fractions were substantially enriched in globulins (about 75 per cent as determined by electrophoresis in the Tiselius apparatus); but they still contain variable amounts of egg albumin, conalbumin, ovomucoid and lysozyme.

In immunological experiments I employed two sorts of antisera: anti-egg-white and anti-egg-globulin preparations (fractions precipitated by ammonium sulphate at 50 per cent saturation). The latter reacts more strongly, quantitatively and qualitatively, than the former, with the globulins of egg-white[4,5].

The results obtained with different techniques are as follows:

By electrophoresis on filter-paper (barbiturate buffer μ 0·1, *p*H 8·2, 6 hr., 4 V./cm.) stained with bromphenol blue, the 'true' globulins are separated from the lysozyme. The latter forms an indefinite trail near the negative end of the paper strip. The egg-globulins give one intensively stained spot, situated between those of egg albumin and conalbumin. The total egg-white and the fractions poor in egg globulins give a faint spot at the same place; the analysis of the 'incomplete egg-white' (artificial preparation, deprived of globulins[3-5]) shows no colour in this position.

By electrophoresis in agar gel (barbiturate buffer, μ 0·05, *p*H 8·2, 5 hr., 4 V./cm.) a larger number of constituents is demonstrated, especially when stained with the 'Amidoschwartz' (black-blue naphthol B 'Geigy'). It is interesting to note that the natural egg-white does not give the same egg globulin spot as the fractionated preparations[6]. Thus, independent of the total protein concentration, the total egg-white analysis revealed only the spot which I have labelled β_2, while my globulin preparations never give this spot, but form the spots β_1 and β_2[6]. Other visible globulin spots are α_1 and α_2; the last correspond to constituents which do not migrate from the original reservoir and the 'tongue' due to lysozyme (an artefact caused by retention of lysozyme near the original reservoir by the agar[4]).

The other dyes employed react differently with the various globulins. For example, azocarmin reacts strongly with the β_1 but very weakly with the β_3. These facts suggest that the available terminal groupings of these two constituents are not the same.

Sudan black did not colour any of the globulins, indicating that they are not lipoproteins.

By specific precipitation by double diffusion in agar plates using the procedure described by me[4,5], numerous lines can be seen, which I attribute to the precipitating systems of egg globulins and their homologous antibodies. There are two kinds of lines: when the concentrations of the antibody and the antigen are near the point of equivalence or an excess of antigen, the first lines appear in 2–3 days near the serum reservoir; the second appears more slowly (6–10 days) and are always near the antigen reservoir. These two kinds of lines correspond to antigens with different diffusion constants, respectively high and low. I have observed one line of the first kind and up to five lines of the second kind. The first line is not apparent with anti-egg-white serum[5].

Table 1

Technique	No. of egg-globulins demonstrated in: Total egg-white	Preparations of egg globulin
Electrophoresis (Tiselius)	2[1] ($G_1 + G_2$)	2
Zone electrophoresis:		
(*a*) Paper	1[2]	1
(*b*) Agar gel	2[5] (α_2, β_2)	4[5] (α_1, α_2, β_1, β_2)
Specific precipitation	1[2]	1[2]
Specific precipitation in agar plates	4–5[4,5]	6[4,5]
Immunoelectrophoresis	3–4[4,5]	9[5]

N.B.—The lysozyme has not been included in this table.

By immunoelectrophoresis, the number of constituents is also dependent on the nature of the serum. Thus, with anti-egg-white serum, the line of β_3-globulin is absent, while it is the principal globulin line with anti-egg-globulin serum.

The number of globulin lines varies with the nature of the fraction studied, but the total number of different lines is at least nine.

The corresponding constituents are classified according to their mobility. I enumerated three α_2 (one of which corresponds to lysozyme), three β_1, two β_2 and one β_3. The lines of α_2 and β_1 are always formed near the antigen reservoir while that of β_3 corresponds to a protein of high diffusion constant.

Sedimentation studies have demonstrated that in my fractions there are constituents of high sedimentation constant ($S_{20} = 15$ and 18).

In conclusion, at least nine globulins have been demonstrated in the chicken egg-white by immunoelectrophoresis; but it is possible that there are more which might be demonstrated with different sera or methods.

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Coagulase Activity *in vivo*

Coagulase production is a property of all pathogenic *Staphylococci* and is the most commonly accepted single criterion of pathogenicity. In addition it has been shown that coagulase plays a part in staphylococcal infections. Evidence for this is indirect: first, clottable plasma inhibits phago-

cytosis of *Staphylococci*[1]; secondly, rabbits can be protected from *Staph. aureus* infection by human coagulase-inhibiting serum[2], and, also, they receive a degree of immunity against such infection by active immunization with coagulase[3].

To our knowledge, however, there is no experimental evidence that coagulase does in fact exercise its clotting action *in vivo* except that in rabbits Tager[4] mentions the occasional fall in blood fibrinogen and death following the intravenous injection of very large doses of coagulase.

The present report presents what is considered to be evidence of *in vivo* clotting by coagulase. The preparation used was a purified coagulase supplied by Dr. E. S. Duthie; this preparation, at a dilution of 1 in 500,000, clotted an equal volume of 1 in 5 human plasma in 1 hr. and no alpha toxin was detected. Chinchilla rabbits (approximately 2 kgm.) were slowly injected intravenously (10–15 min.) with 2–10 mgm. coagulase in 6–8 ml. normal saline. The coagulase effect *in vivo* was assessed in two ways: by the estimation of fibrinogen-levels and histologically.

Fibrinogen was estimated both chemically and electrophoretically. Doses of 2–5 mgm. of coagulase produced a precipitous drop in the fibrinogen-level, the drop being roughly proportional to the amount of coagulase introduced, and the fibrinogen-level at 30 min. after injection ranged from 15 to 40 per cent of the original value. Blood shed at this stage failed to clot and puncture wounds bled freely. The fibrinogen was rapidly re-formed and by the second or third day was twice the initial value or more. Thereafter the level slowly dropped and had returned to the original level at the end of a week. A drop in all globulin fractions was observed simultaneously with the fall in fibrinogen.

Injection of large doses of coagulase (10 mgm.) led to the death of the animals in 10–20 min. Microscopic examination of the organs showed widespread intravascular deposits which gave the staining reactions of fibrin. These deposits were formed of multiple fibrin strands lying parallel to one another and to the long axis of the vessel in which they lay. The deposits were present in small or moderate numbers in the liver, kidneys and adrenals and they were exceedingly numerous in the lung, where they occluded the majority of capillaries and many of the small and large arteries. These findings and the manner in which the animals died suggested that death was due to blockage of the pulmonary vasculature.

The microscopic findings and changes in fibrinogen-level are similar to those observed after the intravenous injection in animals of thrombin or thromboplastin, and in some cases of accidental hæmorrhage in pregnancy.

In control experiments, autoclaved coagulase was used: no fall in fibrinogen-level was observed. Full details of these experiments will be published later.

It appears from these experiments that coagulase, admittedly in high doses, has a potent action *in vivo*. Since purified, but not pure, coagulase was used, it cannot be entirely ruled out that accompanying impurities may be responsible for the changes described above. However, since coagulase is a clotting agent, it seems logical to assume that the disappearance of fibrinogen from the blood and the formation of fibrin deposits in the vessels are due to the action of coagulase itself.

We wish to thank Dr. E. S. Duthie for the generous supply of purified coagulase and Dr. E. B. Hendry and his staff for fibrinogen estimations.

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Anaerobic Uptake of Glucose *in vitro* by the Isolated Rat Diaphragm

THE uptake of glucose *in vitro* by the isolated rat diaphragm has been reported to be the same under both aerobic and anaerobic conditions[1,2]. In these experiments the medium used for incubation was a balanced salt solution buffered with phosphate, and phosphate buffers are known to be inadequate for tissues exhibiting a high rate of glycolysis[3]. The uptake of glucose *in vitro* by the isolated rat diaphragm under aerobic and anaerobic conditions has therefore been re-investigated using as supporting medium a balanced salt solution buffered with bicarbonate.

The diaphragms were obtained from normal, hypophysectomized or adrenalectomized male albino Wistar rats of 100–150 gm. Normal animals were fasted for 20–24 hr. before use, and hypophysectomized or adrenalectomized animals were fasted for 6 hr. After excision the diaphragms were bisected along the central tendon and one half-diaphragm from each animal was prepared and incubated anaerobically, and the other prepared and incubated aerobically. The incubation media used were Geys' bicarbonate-buffered medium[4] and Krebs–Ringer phosphate solution (phosphate-buffered medium)[5]. (The Krebs–Ringer phosphate solution was modified by reducing the calcium content to approximately one-half. The calcium contents of the modified Krebs–Ringer phosphate and Geys' bicarbonate medium were then identical.) The bicarbonate-buffered medium was gassed either with 95 per cent nitrogen, 5 per cent carbon dioxide (anaerobic preparation and incubation) or 95 per cent oxygen, 5 per cent carbon dioxide (aerobic preparation and incubation). Phosphate-buffered medium was gassed either with nitrogen or oxygen. The glucose concentration of the medium was 2·5 mgm./ml. in all instances.

After excision the hemidiaphragms were washed for five minutes in the appropriate medium. The hemidiaphragms were then lightly blotted, transferred to small conical flasks containing 1 ml. of medium, the flasks gassed and sealed, and incubated for 1 hr. at 37° C. in a Dubnoff shaker. After incubation the hemidiaphragms were blotted and weighed and the residual glucose in the medium determined colorimetrically by Somogyi's modification of Nelsons's method[6]. In some experiments the residual glucose was additionally determined manometrically using glucose oxidase, after the method of Keilin and Hartree[7]. Uptake of glucose by diaphragm was calculated as mgm. glucose disappearing

Table 1. Uptake of Glucose *in vitro* by the Isolated Rat Diaphragm under Aerobic and Anaerobic Conditions in Media Buffered with Bicarbonate or Phosphate

State of rat	Incubation medium	Glucose uptake. Mean ± S.E. of mean (mgm. glucose/gm. of wet diaphragm/hr. of incubation)				
		Anaerobic	Aerobic	Difference (anaerobic–aerobic)	t	P
Intact	Bicarbonate-buffered medium	5·68 ± 0·11 (23)	3·03 ± 0·13 (23)	2·65 ± 0·17	15·6	< 0·001
Hypophysectomized		4·96 ± 0·22 (19)	3·54 ± 0·14 (19)	1·42 ± 0·25	5·61	< 0·001
Adrenalectomized		4·52 ± 0·25 (5)	3·04 ± 0·33 (5)	1·48 ± 0·41	3·70	< 0·01
Intact	Phosphate-buffered medium	3·23 ± 0·22 (12)	3·00 ± 0·22 (12)	0·23 ± 0·31	—	> 0·001 —

Figures in parentheses are number of observations from which the mean is derived.

Table 2. Comparison of Glucose Uptakes based on Glucose Values obtained by Copper Reduction (Somogyi, ref. 6) and by Glucose Oxidase (Keilin and Hartree, ref. 7)

Experiment No.	Glucose uptake (mgm. glucose/gm. of wet diaphragm/hr. of incubation)					
	Anaerobic		Aerobic		Difference (anaerobic–aerobic)	
	Copper reduction	Glucose oxidase	Copper reduction	Glucose oxidase	Copper reduction	Glucose oxidase
1	4·15	4·72	2·24	2·87	1·91	1·59
	4·85	5·53	3·26	3·80	1·85	1·53
2	4·38	5·82	1·92	3·36	2·46	2·46
	5·64	6·42	2·38	2·74	3·26	3·68

Each value represents the combined uptake of glucose by five hemidiaphragms incubated together in 3 ml. of bicarbonate-buffered medium.

from the medium/gm. of wet diaphragm/hour of incubation.

The uptake of glucose by the isolated rat diaphragm incubated in bicarbonate-buffered medium was found to be substantially greater under anaerobic conditions than under aerobic conditions (Table 1). The increase in glucose uptake under anaerobic conditions which was seen with diaphragms from normal, hypophysectomized or adrenalectomized rats was highly significant. Since this difference had not been reported by other workers who have studied the uptake of glucose by the isolated rat diaphragm under anaerobic conditions in phosphate-buffered media[1,2] the studies were repeated with a phosphate-buffered medium. In the phosphate-buffered medium the uptakes of glucose under aerobic and anaerobic conditions did not differ significantly—an observation in agreement with those of earlier studies by other workers[1,2], and in clear contrast to the results obtained in a bicarbonate-buffered medium. Measurements of *p*H before and after incubation showed that the *p*H of phosphate-buffered medium fell markedly during incubation under anaerobic conditions (*c.* 0·6 unit) whereas the *p*H of bicarbonate-buffered medium suffered little change (*c.* 0·1 unit).

Anaerobic incubation in a bicarbonate-buffered medium was associated with a significant fall in the level of glycogen in the diaphragm despite the high rate of glucose uptake, whereas aerobic incubation was associated with a significant increase in the level of glycogen. Lactic acid production was significantly increased under anaerobic conditions. Similar changes in the level of glycogen in diaphragm and of production of lactic acid by diaphragm have been noted previously, in phosphate-buffered medium, by Walaas and Walaas[1].

Chain, Catamzaro, Chain, Masi, Pocchiari and Rossi[8] have suggested that reducing substances other than glucose may be added to the medium by diaphragm during incubation and so lead to false values for uptake of glucose when glucose is estimated in the medium by methods based on reduction. In two experiments, therefore, glucose was estimated in the medium both by the copper reduction method of Somogyi[6] and by means of the specific glucose oxidase[7]. The uptakes of glucose, based on glucose values obtained with glucose oxidase, were higher than those obtained by the Somogyi method of glucose estimation. This observation would be in keeping with the suggestion of Chain *et al.* The increase in glucose uptake under anaerobic conditions in the bicarbonate-buffered medium was, however, still evident when glucose uptakes were calculated from glucose values obtained by the glucose oxidase method (Table 2).

These studies indicate that the uptake of glucose by the isolated rat diaphragm is increased under anaerobic conditions in a medium buffered with bicarbonate. The significance of these results in relation to the mode of uptake of glucose by the isolated rat diaphragm will not be discussed here. In a phosphate-buffered medium, anaerobic incubation does not lead to any alteration in the uptake of glucose by the isolated rat diaphragm. Media buffered with phosphate would appear to be unsuitable for *in vitro* studies with the isolated rat diaphragm, because of their poor buffering power. Estimations of glucose by both copper reduction (Somogyi) and by glucose oxidase have supported the suggestion of Chain *et al.*[8] that reducing substances other than glucose are added to the medium during incubation of the isolated rat diaphragm and that these are estimated together with glucose when copper reduction methods are used.

I wish to thank Prof. F. G. Young for helpful advice and criticism; Miss N. Savage for the gift of a preparation of glucose oxidase; and Mrs. J. C. D. Coe for technical assistance. The cost of this work was largely defrayed by a grant from the Medical Research Council.

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Heat Changes during the Clotting of Fibrinogen

In order to get a better insight into the energetics of the clotting of fibrinogen, we conducted heat measurements using the Benzinger[1,2] microcalorimeter.

The heat change during clotting of fibrinogen comes essentially from three sources: (1) the splitting of peptide bonds by thrombin, (2) the neutralization by the buffer system of the charged groups created, and (3) polymerization of the fibrin molecules to a network.

The polymerization involves the formation of 19 hydrogen bonds[3] where the histidine groups appear to be the acceptors[4,5]. In order that the histidines may serve as acceptors at *p*H 6, protons have to be removed. According to Mihalyi[4], at *p*H 6 three protons are removed from histidine residues.

In these experiments bovine fibrinogen, purified according to the method of Laki[6], and Parke–Davis thrombin were used. Usually, the thrombin solution and the fibrinogen solution were dialysed against the same buffer salt solution. About 5 mgm. fibrinogen per ml. was suitable for the measurements. Thrombin was added in an amount sufficient to make the clotting complete in 20–25 min. The experiments were performed in phosphate, tris (hydroxymethyl) amino methane (*tris*) and borate buffers. The results of the experiments are summarized in Fig. 1.

It is seen that in phosphate and borate buffers the heat evolved amounts to about 44 kcal. in a fairly wide *p*H range. In *tris* buffer the heat evolved is higher.

The 44 kcal. of heat evolution found in phosphate buffer at *p*H 7 is practically the same as found by Sturtevant *et al.*[3] for the heat of the polymerization reaction only. From this it follows that the heat of the splitting which is included in our experiments is very small and thus negligible.

At lower *p*H's Mihalyi finds that, as a result of the polymerizations, protons appear to originate from the histidine residues. This process absorbs about 6–7 kcal. of heat per proton. At *p*H 6, where three protons (per mole of fibrinogen, mol.wt. = 330,000) appear, this heat absorption is about 20 kcal. This means that at this *p*H instead of 44 kcal. we would measure 20 kcal. less in the polymerization reaction.

In the total reaction this heat absorption will be compensated by the neutralization heat of the amino-groups generated by the removal of the peptides. In phosphate buffer, therefore, we obtain a line which runs from *p*H 8·5 to 6 at a level of approximately 44 kcal. (Fig. 1).

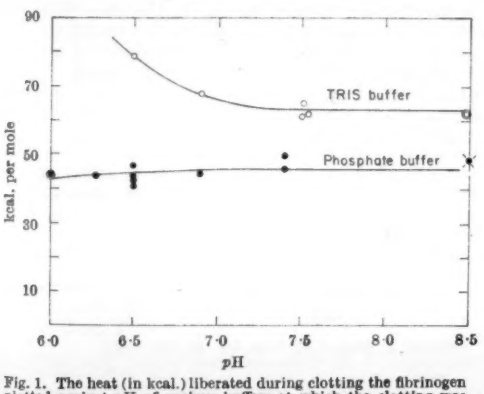

Fig. 1. The heat (in kcal.) liberated during clotting the fibrinogen plotted against *p*H of various buffers at which the clotting was performed. ●, Phosphate buffer; ○, *tris* buffer; ×, borate buffer

In *tris* buffer the situation is different so far as the neutralization of the liberated charged groups is concerned. From *p*H 8 down to *p*H 6 we find that the heat of neutralization of the two carboxyl groups is uniformly about 20 kcal., since *tris* involves about 11 kcal.[3,7] for the neutralization of a proton. The polymerization heat again can be expected to be 44 kcal.; but now as we approach *p*H 6, the three protons removed from the histidine residues are neutralized by the buffer, which involves considerable heat (in contrast to phosphate buffer[3,7]), thus over-compensating the heat consumption needed to remove these protons. We expect the curve, therefore, to bend upward, but to run about 20 kcal. higher (between *p*H 7–8·5) than the results obtained in phosphate buffer. The 20 kcal. difference is the result of the neutralization of the two protons of the carboxyl groups which are liberated during the enzymatic phase.

These experiments definitely indicate, then, that two (but not more) peptide groups are split during the clotting of fibrinogen. It is expected, therefore, that the peptides split from fibrinogen should contain C-terminal groups. This is in agreement with recent experiments of Gladner and Laki (unpublished work) showing that carboxypeptidase brings about a considerable degradation of both of these peptides. A detailed account of the work will be submitted for publication elsewhere.

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Cell Membranes and Morphogenesis

Cell membranes can be readily visualized in the electron microscope; but a rather special cell system is needed if one wishes to study their supposed role[1,2] in morphogenesis. In the hair follicle we have been able to examine at high resolution a system which fulfils most of the electron microscopist's demands. It is small enough not to make the task of surveying it at high magnification too formidable and, in a geometrical sense, simple, in that the differentiating

cells move away from the papilla in almost linear streams, preserving the order of their formation.

In normal growth a steady stream of cells, maintained by division in the neighbourhood of the papilla at the base of the follicle, passes up the tube formed by the outer root sheath and differentiates to form as many as six concentric cylinders; the three outer cylinders constitute the inner root sheath and the three central, the hair proper. The cells of these layers are differentiated in their shape and in the different intracellular materials which they make.

In the mid bulb immediately above the zone of cell division the plasma membrane, seen in material fixed in osmium tetroxide solution and embedded by standard electron microscopical procedures, consists of a single thin (<50 A.) dense line bounding the cytoplasm. The cell surfaces are extremely convoluted and long finger-like pseudopods may penetrate far into neighbouring cells. These fixed appearances probably record momentary aspects of the restless membrane activity often noted in films of cultured cells. One gains the impression that adhesion between cells is slight. The intercellular space often dilates into wide empty openings (up to 2–3μ wide); where the membranes are closer it is evident (Fig. 1) that the gap is actually filled by a material of lower electron absorption than that of the membranes. Over certain small areas the separation is more constant (125–150 A.), and these seem to correspond to areas of true adhesion with the intercellular material acting as a cement. Such localized contacts also characterize the epidermis[3,4] and outer root sheath.

The first signs of differentiation appear in the presumptive cuticle cells and are shown by a spread of the 'adhesive contacts' leading to a closing of the gaps, a smoothing out of the cell surfaces and the progressive assumption of a columnar habit by the cells. This development also occurs later and to a lesser degree in the sheath cells. In the cortex, however, contact areas remain small and local, membrane activity persists and the intercellular gaps afford pathways for melanocyte processes bearing pigment. The fully established contacts between the cuticle cells seem, however, to bar further peripheral penetration by the pigmented processes, and the cuticle and sheaths thus remain unpigmented.

At about the level of the tip of the papilla all the cells (except those of the cuticle) have begun the synthesis of their characteristic products: fibrils of keratin in the cortex and droplets of amorphous trichohyaline in the inner root sheath. Trichohyaline synthesis commences first and proceeds farthest in the Henle cells nearest the outer root sheath; it is delayed and less marked in the two inner layers of the sheath. In each of these three cell layers, and with a time-lag between each, the amorphous trichohyaline droplets suddenly transform into a birefringent fibrous modification, a change well shown electron microscopically, and at the same time the cell membranes separate to about 250–300 A. with the deposition between them of a dense central layer. This type of membrane modification occurs also in the cuticle cells and leads to the deposition of a most elaborate succession of coats between the cells (Fig. 2). Proceeding from one cell to the other (and counting the 'white' lines which represent material of low electron density) we have here certainly seven layers and perhaps even nine.

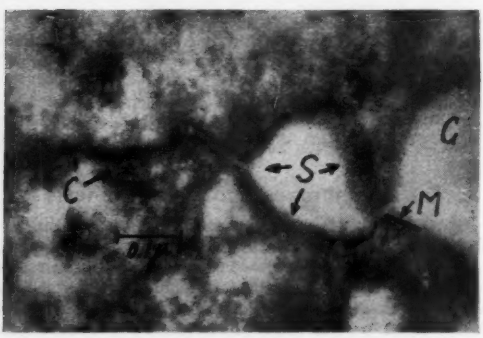

Fig. 1. Portions of two cells in the mid bulb of the hair follicle showing the nature of the areas of contact *C*. *G*, an intercellular gap; *S*, intercellular cement; *M*, the plasma membrane. (× 116 000)

Fig. 2. Membrane complex developed between two cuticle cells at the level of keratin formation. *K*, keratin droplets; *M*, plasma membranes. (× 120,000)

In the central fibrous cortex of the hair the membranes, which have persisted in their surface activity longer than elsewhere, finally dilate and become cemented together as the cells fill with fibrous keratin, but do not develop a complex layered structure.

Surveying the whole process, it is seen that everywhere changes in cell contacts accompany differentiation. In the bulb localized adhesion, spread of contacts and suppression of membrane activity (contact inhibition[5]) seem early formative events in the causal chain; the later more elaborate development of the membranes seems part of the process of consolidating the tissue.

This investigation has been supported by grants to the Chester Beatty Research Institute (Institute of Cancer Research: Royal Cancer Hospital) from the British Empire Cancer Campaign, Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

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A New Method for the Identification of Biochemical Mutants of Micro-organisms

A RAPID method for the identification of biochemical mutants of *Ustilago maydis* has been devised. The method is suitable for sporing or non-mycelial micro-organisms which form discrete colonies on agar.

Thirty-six possible requirements for single growth-factors are tested. Twelve plates of minimal medium are each supplemented with different combinations of six growth-factors with the arrangement shown in Table 1. A mutant strain with a single biochemical requirement when inoculated on all twelve plates will grow on two of them, one of plates 1–6 and one of plates 7–12. Thirty-six combinations are possible; each combination indicates a different requirement. The number of requirements tested can be varied by altering the number of plates and the arrangement of growth-factors among them.

Table 1

		Plates 1	2	3	4	5	6
	7	adenine	biotin	phenylalanine	alanine	arginine	leucine
	8	hypoxanthine	folic acid	serine	cysteine	ornithine	glycine
	9	cytosine	pantothenic acid	tryptophan	threonine	aspartic acid	*iso*leucine
Plates	10	guanine	pyridoxin	tyrosine	thiosulphate	proline	histidine
	11	thymine	thiamin	*p*-amino benzoic acid	methionine	glutamic acid	lysine
	12	uracil	riboflavin	nicotinic acid	choline	inositol	valine

An inoculating instrument with twenty-five points is used for transferring cells from each of twenty-five different mutant colonies growing on complete agar medium to each of the twelve plates. The multiple inoculator consists of twenty-five bolts ($\frac{1}{8}$ in., 10 *BA*) fitted to double-thickness zinc gauze. A short handle allows the instrument to be sterilized by dipping in methylated spirit and flaming. In preparing the master plate of complete medium the mutants are inoculated in positions corresponding to the points of the inoculating instrument and then incubated until a suitable growth has occurred. The Lederbergs' technique of replicating colonies with velvet or damp filter paper would be an equally suitable method for carrying out the inoculations[1].

So far as possible the arrangement of growth-factors allows for the detection of likely double or alternative requirements. Mutants requiring, for example, both *iso*leucine and valine for growth will only grow on plate 6, and the precise requirement must be tested with different combinations of the six growth-factors in that plate. Mutants with alternative requirements will grow on more than two plates. For example, those using methionine or cysteine will grow on plates 4, 8 and 11, and their requirements can be detected at once.

When large numbers of mutants are to be identified, this technique is more efficient than previous methods in which the field of search is progressively reduced[2,3]. With one or a few mutants auxanographic techniques are preferable[4,5].

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The Snail's Foot as a Langmuir Trough

THE importance of the surface film of protein on stationary or slowly moving bodies of water as a food for small aquatic animals had apparently not been realized until the recent work of Goldacre[1], who made film-pressure measurements on ponds, lakes and rivers and found on all of them unimolecular layers of protein in higher or lower states of compression. A concomitant study of the behaviour of small aquatic animals led him to the conclusion that they ate this protein in large amounts. Observations of the movements of dust particles in a film during its ingurgitation by a tadpole indicated that this animal might well eat its own dry weight of protein, spread as a monolayer at the air–water interface, in one day.

I have recently acquired, through the courtesy of Mr. G. Ashby of the Zoological Society of London, some water snails of the South American species *Pomacea canaliculata*. Studies of the behaviour of these animals, of which my largest specimen weighs 52 gm., have shown that they not only eat surface films of protein, but also have the technique of compressing them to fibrous masses which are then eaten without a disproportionately high intake of water.

The phenomenon is manifested in the following manner. A snail in the usual resting position, adhering to the wall of the tank or to a floating plant just below the water surface, detaches the anterior portion of its foot and extends and curves it in such a manner as to form, either alone or with the tank wall, a funnel with its rim in the surface. Rapid undulatory movements are then seen to pass posteriorly from the periphery of the foot, while from the motion of particles in the adjacent water surface it is clear that the material constituting the surface film is being drawn towards the mouth of the funnel. Within a few seconds the presence of a collapsed protein film is evident at the water surface within the funnel. As the protein accumulates, the water-level is forced down and after, say, 10 sec., the funnel is almost empty, with denatured protein tightly packed in the narrow end. After a short period of further accumulation, the animal brings its mouth forward and downward and eats the protein.

The funnel is not refilled from above during compression of the film since the foot is rendered hydrophobic by the protein and the contact angle between foot and water is hence increased. The protein is probably anchored to the mucin layer of the foot by its polar side-chains, the hydrophobic, non-polar groups being directed predominantly towards the air. The strongly anionic character of the mucin is shown by the avidity with which, *in situ*, it takes up basic dyes such as methylene blue.

This behaviour is very much more frequent in young snails than in adults. With the latter, film compression sometimes occurs, as it were, absent-mindedly, while the animal is engaged in a clearly

more rewarding pursuit such as the consumption of a lettuce leaf. In such an event the protein mass is abandoned.

It may be pointed out that proteins are the only quantitatively important biological materials that yield surface films capable of pedipulation in the fashion here manifested.

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Influence of Freezing-rate on the Denaturation of Cold-stored Fish

It is commonly held that the major factor governing the changes which gradually take place in frozen muscle is the temperature of storage, and that the speed at which the tissue was originally frozen is of relatively small importance. Though storage temperature is undoubtedly the biggest single factor, it now appears that freezing-rate is more important than was formerly supposed.

Examination of published work relating to the effect of freezing-rate on fish after cold storage shows that in most cases this rate is very arbitrarily defined. At the worst, the only information given is the temperature of the medium in which material to be frozen is placed. A better concept is the 'freezing-time' defined as the time taken for a certain part of the muscle to pass through two fixed temperatures as measured by thermocouples. However, the tendency is still to relate observations to a simple numerical value, without intimate knowledge of corresponding disposition of the ice crystals or any cell damage for which they may be responsible.

It was the aim of the present work to investigate denaturation in relation to the disposition of the ice in fillets of North Sea cod (*Gadus callarias*). The type of ice distribution was indicated indirectly by a recent technique, which utilizes the amount of deoxyribose nucleic acid in the intercellular fluid as a measure of the amount of cell damage[1,2]. Denaturation was assessed from the percentage of muscle proteins that would dissolve in neutral 5 per cent sodium chloride. The reproducibility and accuracy of this method was much enhanced by taking account of most of the biological variation which normally destroys much of its usefulness. The technique by which this was done has recently been described[3]. Fillets were frozen at different speeds by stacking them in vertical piles on an aluminium plate maintained at −78° C. by solid carbon dioxide. It had previously been found[4] that such an arrangement yielded fillets frozen over a suitable range of conditions, those in contact with the plate freezing most quickly, and those at the top of the stack most slowly. Observations at the time of writing have been limited to fillets afterwards stored at −14° C. for 86, 108, 148 and 162 days, and at −30° C. for 328 and 390 days.

While the overall extent of denaturation depended on the length of storage, the results showed clearly that large differences in denaturation existed between fish frozen at different rates. Denaturation was relatively low where high-speed freezing produced small intracellular ice columns. It increased steadily with slower freezing to a maximum value at the point

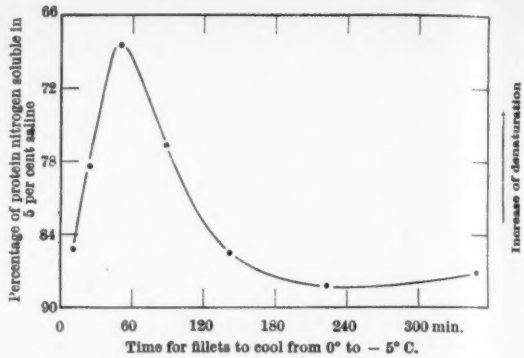

Fig. 1. Percentage of cod muscle proteins which can be dissolved in 5 per cent sodium chloride after freezing fillets at different rates and storing them at −30° C. for 390 days

where the largest possible intracellular ice columns were produced, the proteins being then compressed into narrow strips along the margins of the cells (*see* Love[1], picture *E*). As freezing became slower still, cells were burst open, denaturation decreased, and decreased still more when the ice commenced to form in the intercellular spaces, until at freezing-times of 200–250 min. (time to cool from 0° to −5° C.), where all ice was intercellular and fibres no longer ruptured, denaturation was at a minimum. There was a gradual increase in denaturation after very slow freezing (500 min. and upwards), probably the result of dehydration, the ice front moving so slowly that osmosis was occurring from the cells outwards. An important factor affecting denaturation seems, therefore, to be the mode of ice formation and distribution and the resulting concentration patterns of tissue salts, rather than actual mechanical damage to the cell walls.

The results from storage at −30° C. for 390 days are shown in Fig. 1, which illustrates the considerable difference in denaturation between fish frozen in 70 and 220 minutes. By deoxyribonucleic acid measurements the change-over from intra- to intercellular freezing was shown to have commenced in fillets with a freezing time of 60 min. and to have been complete in those of 130 min. freezing time in this experiment. The smoothness of the curve underlines the accuracy of the denaturation measurements. This pattern was not shown by fillets that had been stored at −14° C. for 162 days, since denaturation was almost complete at all rates of freezing. It is significant that the quantity of expressible fluid obtained under standard conditions from these fillets was almost the same at each rate of freezing, suggesting that the usefulness of such determinations is limited.

An indication of relative toughness can be obtained from a taste panel, and preliminary data obtained in this way suggest that the relation between toughness and denaturation is not a simple one, at any rate at low storage temperatures. For example, in Fig. 1, at a freezing-time of 220 min., 88·2 per cent of the proteins are soluble—a value but little below that of fresh fish (95–96 per cent)—but the muscle is undoubtedly tough to eat. This finding is in accord with the work of van Mameren[5], who detected no reduction in protein solubility at this temperature, in spite of increased toughness. Toughness and solubility appear to be more closely related at about −10° C.[5,6].

It would appear that these phenomena have previously been overlooked on account of the relatively narrow range of conditions under which they occur.

A full account of the completed work will be published elsewhere.

Protein solubilities were determined by Mr. J. I. M. Ironside and Mr. I. Robertson. Nucleic acids were determined by Miss Eleanor Brown. The work described in this communication is part of the programme of the Food Investigation Organization of the Department of Scientific and Industrial Research.

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Protective Action of Vitamin B_{12} in Experimental Liver Injury

THERE are several reports concerning the biochemical changes accompanying experimental liver damage by administration of carbon tetrachloride and other steatogenic poisons. However, the fundamental metabolic deviation causing fatty degeneration has not been well understood. Patwardhan *et al.*[1] have demonstrated that marked changes in the distribution and quantity of several constituents of the liver cells occur before structural damage to the organ. In the present communication, it is shown that a rapid rate of depletion of soluble sulphydryl compounds is among the major derangements in liver injury by carbon tetrachloride. The possibility has been indicated that the protection afforded by prior administration of vitamin B_{12} may be due to its known influence on sulphydryl metabolism[2].

Adult male rats (Wistar strain), 100–150 gm. in weight, reared on the laboratory stock diet, were given, intraperitoneally, vitamin B_{12} (10 μgm./animal) 3 hr. prior to carbon tetrachloride administration (2 c.c. per kgm. body-weight). It was ascertained from preliminary experiments that protection by the vitamin was best under these conditions and that animals not receiving the vitamin showed maximum liver fat accumulation at the end of about 48 hr., after which there was regeneration. Animals were killed at intervals after carbon tetrachloride injection and the livers quickly excised, chilled and homogenized in cold isotonic sucrose to a 20 per cent suspension. Determinations were made on aliquots of the whole liver and on centrifugally separated fractions. The values reported (Table 1) are averages for four animals from each group and are for the whole liver only, sampled at the end of 6 and 48 hr. after carbon tetrachloride poisoning and employing the analytical procedures cited.

It is seen that liver fat accumulation proceeds even after restoration of glutathione to normal levels and that vitamin B_{12} protects against rapid depletion of glutathione. A study of the distribution of glutathione in cell fractions has shown that while the mitochondrial fraction is completely devoid of it, nearly 80 per cent is present in the supernatant, the remainder being accounted for in the nuclei. Nuclear bound glutathione does not become depleted as a result of carbon tetrachloride injury. Mitochondrial damage in carbon tetrachloride injury can be inferred from alterations in pyridino-protein nucleotides[8] and lability of other acid-soluble nucleotides[9].

The protective action of vitamin B_{12} is more marked with respect to changes in ribonucleic acid and in phospholipids than in neutral lipids. It has apparently no effect on glycogen losses in the prenecrotic and necrotic stages. Deoxyribonucleic acid and methionine values remain unchanged throughout.

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Lability of Intramitochondrial Components in Experimental Liver Injury

THE mitochondrial membrane has a limited ability to retain nucleotides and other co-factors like Mg^{++} which are essential for maintaining normal respiration and efficient coupled phosphorylation[1]. Exposure to hypotonic conditions, ageing, other environmental alterations and physiological states cause swelling of the mitochondria accompanied by biochemical modi-

Table 1. CHANGES IN LIVER CONSTITUENTS IN INJURY BY CARBON TETRACHLORIDE

	Untreated control	Hours after administration of carbon tetrachloride			
		6		48	
		Without vitamin B_{12}	Vitamin B_{12}-protected	Without vitamin B_{12}	Vitamin B_{12}-protected
		(mgm./gm. fresh weight)			
Total lipids (ref. 3)	23·6 ± 1·5	29·1 ± 1·2	28·2 ± 1·1	48·8 ± 2·5	34·9 ± 1·5
Phospholipids (ref. 3)	15·1 ± 0·2	15·1 ± 0·3	15·5 ± 0·2	10·6 ± 0·2	14·6 ± 0·2
Ribonucleic acid (ref. 4)	10·6 ± 0·6	8·8 ± 0·6	9·4 ± 0·6	6·9 ± 0·9	10·3 ± 0·3
Deoxyribonucleic acid (ref. 4)	3·8 ± 0·3	3·6 ± 0·3	3·7 ± 0·3	3·6 ± 0·3	3·6 ± 0·3
Glutathione (ref. 5)	1·4 ± 0·2	0·4 ± 0·2	1·3 ± 0·2	1·2 ± 0·1	1·7 ± 0·1
Glycogen (ref. 6)	3·3 ± 0·5	1·0 ± 0·2	1·5 ± 0·3	0·7 ± 0·2	0·6 ± 0·4
Methionine (ref. 7)	5·0 ± 0·5	4·9 ± 0·5	5·0 ± 0·3	4·9 ± 0·3	5·0 ± 1·0

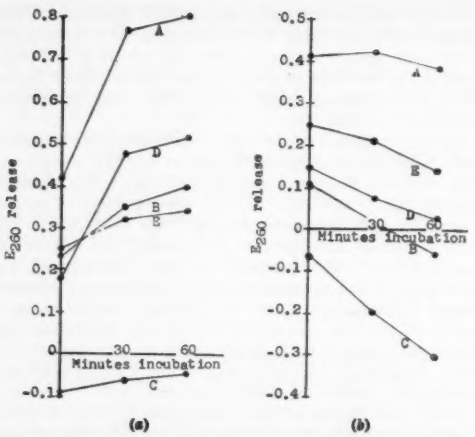

Fig. 1. (*a*) Release of acid-soluble nucleotides from mitochondria incubated in phosphate buffer; (*b*) effect of oxidative phosphorylation on E_{260} release.
A, Normal mitochondria; *B*, mitochondria from livers 6 hr. after injury by carbon tetrachloride; *C*, mitochondria from livers 48 hr. after injury by carbon tetrachloride; *D*, as in *B*, vitamin B_{12}-protected; *E*, as in *C*, vitamin B_{12}-protected

fications, such as loss of Mg^{++} and of acid-soluble nucleotides with absorption maximum at 260 mμ, increase in adenosine triphosphatase activity and dissociation of phosphorylation from oxidation[1–3]. Conditions favourable to oxidative phosphorylation or the presence of adenosine monophosphate apparently protect the mitochondria against this damage[1,4].

Uncoupling of oxidative phosphorylation has been reported in thyrotoxicosis[5], dietary necrotic liver degeneration[6] and experimental liver injury[2]. Mitochondrial preparations from such liver tissues show lowered oxygen consumption and decreased levels of pyridine nucleotides[2,5]. It was of interest to study their behaviour with respect to release of nucleotides and to ascertain the influence of prior administration of vitamin B_{12}, which protects against thyrotoxicosis[7] and injury by carbon tetrachloride[8]. This report relates to observations with the steatotic poison.

Well-fed adult rats (Wistar strain), 150–200 gm. in weight, were used for the different groups (Figs. 1*a* and *b*). Carbon tetrachloride was administered intraperitoneally at 2 ml. per kgm. body-weight, and control animals were similarly given corresponding amounts of distilled water. Vitamin B_{12} was also given intraperitoneally at 10 μgm. per animal, 3 hr. before carbon tetrachloride injection. The animals were killed by decapitation, 6 and 48 hr. after injury by carbon tetrachloride[8]. Mitochondria from the livers were prepared by the procedure of Schneider and Hogeboom[9]. The mitochondrial pellet was taken up in cold isotonic sucrose and aliquots equivalent to 500 mgm. wet weight of liver were incubated in the presence of 0·01 *M* phosphate buffer, *p*H 7·2, either alone or, to maintain conditions for oxidative phosphorylation[1], with additions of 3 μmol. each of magnesium chloride and adenosine monophosphate and 30 μmol. of glutamate in a final volume of 4·0 ml.; powdered sucrose was added to give isotonic conditions. At commencement, as well as at the end of 30- and 60-min. intervals, the suspensions were spun at 7,500 × *g*. The supernatant was deproteinized with 2 ml. of 1·5 *N* perchloric acid and the optical density at 260 mμ of the resulting solution was read in a Beckman *DU* spectrophotometer (Figs. 1*a* and *b*). Results are averages of at least quadruplicate determinations in each group.

As may be expected, incubation of mitochondria from normal livers in phosphate buffer results in a loss of intramitochondrial nucleotides which is checked in the presence of the oxidizable substrate. In mitochondria from steatotic livers the initial release of E_{260} material is very low and points to damage to mitochondrial morphology *in vivo*. There is a non-specific interference from absorption due to Mg^{++} and PO_4''', the influence of which are apparently more pronounced with mitochondrial preparations from livers 48 hr. after administration of carbon tetrachloride.

The uptake of adenosine monophosphate from the medium in presence of glutamate could be due to the action of surface adenylate kinase and is consistent with the suggestion[2] that steatotic poisons interfere with the mechanism whereby inorganic phosphate is transferred to adenosine diphosphate to form adenosine triphosphate coincident with oxidation rather than with adenylate kinase action.

The protective action of vitamin B_{12} against poisoning by carbon tetrachloride[8] is reflected in the initially higher release of E_{260} material of mitochondrial preparations, as well as in its more normal increased release with time to the surrounding medium. This protection may not be specific and could arise from the general lipotropic action of the vitamin and from its known influence on sulphydryl conservation and nucleotide metabolism.

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Diphenylhydantoin and Brain-Levels of 5-Hydroxytryptamine

It has been demonstrated that the anti-epileptic drug, diphenylhydantoin ('Phenytoin'), in rats is capable of inhibiting the pituitary–adrenal system, preventing the usual depletion of adrenal ascorbic acid by such stresses as unilateral adrenalectomy, intravenous vasopressin and subcutaneous epinephrine[1].

There is evidence to suggest that 5-hydroxytryptamine might be an important neuroregulatory amine, perhaps playing a part in the transmission of impulses in the brain. It has been established that 5-hydroxytryptamine is present in certain areas of the brain[2,3], and that many of these regions are capable of synthesizing 5-hydroxytryptamine[4]. The hypothalamus, an area of extreme importance in autonomic and possibly hormonal homeostasis in the organism, is one region with high levels of 5-hydroxy-

tryptamine and the enzyme responsible for its formation.

It seemed of some interest to determine the effect of diphenylhydantoin upon brain-levels of 5-hydroxytryptamine, since to date the only substances reported to alter brain-levels of 5-hydroxytryptamine have been, on one hand, the monoamine oxidase inhibitor, iproniazid[5], and the immediate precursor of 5-hydroxytryptamine, 5-hydroxytryptophan[6], which lead to an increase, and, on the other hand, reserpine, rescinnamine and 11-demethoxyreserpine, which lead to a decrease, in brain 5-hydroxytryptamine[7,8].

In preliminary experiments it was found that rats treated with diphenylhydantoin (100 mgm./kgm. B.I.D., intraperitoneally for two days) had twice the normal brain-level of 5-hydroxytryptamine (see Table 1). A further increase in the elevation occurred after the administration of 5-hydroxytryptophan (100 mgm./kgm. intraperitoneally given to diphenylhydantoin-treated rats). These animals were killed 1 hr. after receiving 5-hydroxytryptophan, and the adrenal ascorbic acid level was found to be lowered (no such result was obtained in control animals treated with the slightly alkaline medium in which 5-hydroxytryptophan was dissolved).

Table 1

Primary* treatment	Secondary treatment	Adrenal ascorbic acid† (μgm./100 mgm. adrenal)	5-Hydroxytryptamine† in brain, (mμgm./gm.)
None	None	460 (25)‡	330 (25)
Diphenylhydantoin	None	426 (12)	682 (6)
Diphenylhydantoin	One adrenal removed, and 1 hr. later the second taken for analysis	426 (10)	—
None	5-HTP 100 mgm./kgm. i.p. 1 hr. previously	—	879 (5)
Diphenylhydantoin	5-HTP 100 mgm./kgm. i.p. 1 hr. previously	374 (9)	1,290 (6)
None	Reserpine 2·5 mgm./kgm. s.c. 6 hr. previously	364 (5)	100 (3)
Diphenylhydantoin	Reserpine 2·5 mgm./kgm. s.c. 6 hr. previously	413 (2)	245 (2)

* In these experiments, male rats 150–225 gm. were used. The diphenylhydantoin was administered intraperitoneally 100 mgm./kgm. twice daily for four doses.

† Bioassay of 5-hydroxytryptamine was on hearts of *Venus mercenaria*: acetone extracts of whole brain (excluding cerebellum) made by procedure of Amin, Crawford and Gaddum (ref. 2). Ascorbic acid was determined by method of Roe and Kuether (ref. 9).

‡ Figures in parentheses indicate the number of rats.

Reserpine (2·5 mgm./kgm. subcutaneously) caused the same degree of depletion of brain 5-hydroxytryptamine in diphenylhydantoin-treated rats as in untreated animals when examined at 6 hr. after administering reserpine. However, there was no apparent depletion of adrenal ascorbic acid in the diphenylhydantoin-treated animals, in contrast to the regularly observed decrease seen in normal control animals. In control animals reserpine caused a more marked depletion of adrenal ascorbic acid at 2 and 4 hr., whereas in a small group of diphenylhydantoin-treated animals no significant changes were determined at these times.

Further examination of these interesting relationships are being undertaken; but it is clear that in the rat diphenylhydantoin causes an increase in the level of 5-hydroxytryptamine in the brain.

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Shikimic Acid in Apple Fruits

Following the discovery of quinic acid in apple fruits[1] it has been found in other fruits[2,3] and in grass[4]. It was originally suggested that quinic acid might provide a link between aliphatic and aromatic metabolism in plants, and that shikimic acid might be the first stage from quinic acid in the 'disaturation' of the six-membered carbon ring[1]. However, shikimic acid could not at that time be found in apples. It was, however, isolated later from grass[5] and has recently been detected in small amounts in the juice of cider apples by Phillips, Pollard and Whiting[6], who used paper chromatography and a specific colour reaction. The development of the technique of gradient elution of organic acids from anion exchange resins[7,8] has greatly facilitated the separation and isolation in the pure state of organic acids present in very small amount from solutions which also contain other acids in much larger quantity; by using this technique, an acid has now been found in very small amount on paper chromatograms prepared from extracts of the peel of Bramley's Seedling apples which gave a yellow to orange colour with Cartwright and Roberts reagent[9] (specific for quinic, shikimic and dihydroshikimic acids[6]) and corresponded in R_{Malic} values with shikimic acid. About 20 mgm. of this acid was obtained in the pure form from an extract of 300 gm. of the peel of the same apples using gradient elution (acetic acid) from 'Dowex 1' columns in the acetate form. The acid had a specific rotation of $[\alpha]_D^{20} = -177{\cdot}5°$ (an authentic sample, measured at the same concentration, of shikimic acid kindly supplied by Dr. Wayne Umbreit of the Merck Institute, gave $[\alpha]_D^{20} = -177{\cdot}1°$). The elementary analysis gave, C, 46·9; H, 5·8 per cent; calculated for shikimic acid C, 48·3; H, 5·79 per cent. The specimen had a melting point of 182·5° C. (corrected); mixed melting point with the Merck sample of shikimic acid, 183·5° C. (corrected). It was undoubtedly shikimic acid.

The acid is barely detectable in the peel of unripe apples; but it increases in amount as the fruit ripens and becomes senescent. The amount of shikimic acid in pulp tissue even from senescent fruit is extremely small. It is interesting that there is also much less quinic acid in the pulp than in the peel of comparable apples[1,6]. If quinic and shikimic acids

are indeed concerned in a chain of reactions leading to full aromatization of the six-carbon ring, it is possible that the rate of conversion of shikimic acid to the next member of the sequence is greater than the rate of production of quinic acid, so that shikimic acid appears in detectable amounts only during the general slowing down of metabolic activity associated with the senescence of the fruit.

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Physiological Control of Population Growth

Mouse ova collected from the Fallopian tubes at the eight-cell stage have been consistently shown to develop to blastulæ when cultivated in a purified medium[1]. It has now been observed that if progesterone is added to this medium, all ova die when the concentration is 8 μgm./ml. or more. A proportion survive at 4 μgm./ml., while a concentration of 2 μgm./ml. is without apparent effect. Since Forbes[2] found a level of 5·2 μgm./ml. in human plasma it seemed possible that this action of progesterone, together with those described by Pincus[3] and Ishikawa[4], might provide a method of fertility control. However, when recently inseminated mice were injected with 10 mgm. of progesterone intraperitoneally on two successive days, there was no reduction in the number of free blastulæ or of implantation sites.

The development of blastulæ from tubal ova *in vitro* was also prevented by low concentrations (10 μgm./ml.) of 'Triton' *W.R.* 1339 and other surface-active agents. In the presence of these substances the blastomeres, which normally fuse to form a compact spheroidal mass, failed to do so and remained discrete and rounded. The concentration required to produce this change was considerably less than that maintained in the blood by Cornforth *et al.*[5], or used in cultures of monocytes by Mackaness[6], which indicates that ova are more sensitive than other tissues to the action of 'Triton'. None the less, normal blastulæ could be recovered from the Fallopian tubes of mice injected intraperitoneally with 25 mgm. of 'Triton' on two successive days shortly after mating. In these animals, however, implantation did not occur, and if the injections were delayed until it had taken place the embryos were aborted or resorbed. A single intraperitoneal dose (10 mgm.) of suramin prevented or interrupted pregnancy in a similar way.

It is possible that this action of 'Triton' is related to the depletion of lipoids of the corpus luteum described by Rees[7]; however, such depletion did not occur in the animals injected with suramin. Nevertheless, both these substances are active in the systems described by Lovelock and Rees[8], so that their action in this case may also be related.

The absence of any action of 'Triton' or progesterone on ova *in vivo* may be due to a failure of the substances to reach the lumen of the Fallopian tubes. If this can be overcome, it may be possible to interrupt the course of pregnancy at the stage of oval cleavage.

The finding of an undescribed pharmacological action of suramin after years of clinical use is disquieting, and suggests the need to test new drugs on pregnant animals.

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Influence of Light on Sporulation of Brewing Yeast

It is well known that bottom yeast as used in the brewing industry can scarcely be made to sporulate. Only a few strains produce some spores. This is a handicap in experiments devised to obtain improved yeast by crossing suitable strains.

In this laboratory many of the presporulating and sporulating media described in the literature were tried with rather poor results. On the other hand, the influence of the season was observed: as a rule, more spores were formed in winter and spring.

Winge has shown that the formation of spores indicates a change from the vegetative generation to the generative generation of the life-cycle of the yeast. Now in the higher plants light has a considerable influence on this transformation. There are plants which only flower when exposed to a long period of light, others are short-day plants. Finally, there is a group which is indifferent to light. Influence of light on the sporulation of yeast was therefore investigated.

Several bottom yeasts, which are still in use in breweries, were inoculated in tubes with about 20 ml. of sterilized wort. After 7 days, when fermentation had ceased, the yeasts were transferred to new tubes. After 2 days, when fermentation was vigorous, 1–2 ml. of the wort was transferred to gypsum blocks.

After the wort had penetrated into the gypsum blocks the Petri dishes were provided with sterile tap-water. After 5 days, preparations of the yeasts on a slide stained with malachite green and safranin were examined microscopically.

One set of cultures (the dark set) had been kept in a dark thermostat at 20° C. all the time.

The second set (the long-day set) had been kept in the window. The third set (the short-day set) had been placed in the window from 9 until 17 hr. and for the rest of the time stored in the dark thermostat at 20° C. The dark set was not exposed to light except when being inoculated in normal daylight. The short-day set was subjected to 8 hr. daylight, the long-day set to about 16 hr., as the experiments were performed in May and June.

The culture tubes as well as the gypsum blocks of one set were kept under the same conditions.

Table 1

Yeast	Exposure time (hr.)	No. of cells counted	Percentage vegetative cells	Percentage asci with 1 sp.	2 sp.	3 sp.	4 sp.	Total asci (per cent)
G_{2a}	0	566	98·0	0·2	0·9	0·9	0	2·0
	8	605	96·4	0·8	1·0	1·5	0·3	3·6
	16	323	54·5	9·3	13·0	16·4	6·8	45·5
G_4	0	489	57·1	2·0	18·6	9·6	12·7	42·9
	8	610	75·9	2·1	7·0	9·7	5·3	24·1
	16	615	89·5	1·3	3·1	4·3	1·8	10·5
G_{17}	0	601	97·2	1·5	0·7	0·5	0·1	2·8
	8	620	97·7	1·0	1·1	0·2	0	2·3
	16	633	96·6	2·3	0·9	0·2	0	3·4

Three typical examples of the results are given in Table 1.

Sometimes when the experiments were repeated several times the results were identical; although at other times the results were different. Perhaps there is a certain period of sensitivity to light that may have a conclusive influence; but this has not yet been investigated. No doubt there exists an influence of light in inducing sporulation in the yeast strain G_{2a}. In other strains the sporulation is inhibited as shown in the case of strain G_4. The third type is indifferent towards light, as the latter neither stimulates nor inhibits sporulation (G_{17}). This was, however, only found with badly sporulating yeasts. On the other hand, no abundantly sporulating bottom yeast is known.

When the water of the 5-day-old cultures on gypsum blocks was replaced by a 0·1 per cent glucose solution, the sporulation sometimes could be improved without altering the proportion of the results. In one experiment 0·5 per cent sodium acetate produced no improvement.

The experiments will be extended with more exposure times. Where there is a sensitivity towards light, a substance, presumably a pigment, is probably responsible. This is to be investigated. With regard to this substance, the effectiveness of different wavelengths will be also examined.

Some strains show an influence of light on the rate of fermentation. When the cultures of these yeasts are exposed to artificial light during 24 hr. the rate of fermentation is decreased. This inhibition may explain the irregular results which are sometimes obtained.

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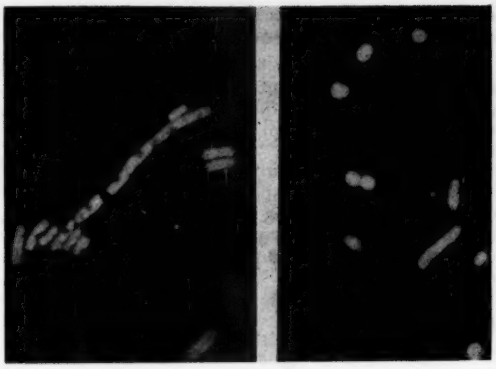
Autolytic 'Protoplast' Release in *Bacterium coli*

We recently discovered accidentally that controlled autolysis of certain Gram-positive bacteria in concentrated sucrose solutions adjusted to a critical ionic strength at *p*H 6 results in the release of the internal protoplasts from the mechanical protection of the cell-wall[1,2]. These 'protoplasts' are stable in suspension media of osmotic pressure above 20 atm., but lyse in more dilute media. The observations of Alfred Fischer[3] and Garbowski[4] on plasmoptysis of certain Gram-negative bacteria in media of low salinity suggested that autolytic release of stable protoplasts might also be possible in these organisms. We have therefore made a preliminary investigation of the conditions required to release the protoplasts of *Bacterium coli* (American strain *B*).



(*a*) (*b*)

Fig. 1. Anoptral contrast micrographs of *Bacterium coli* (*a*) at commencement of incubation and (*b*) after 12 hr. incubation in the controlled autolysis medium (× 4,000)

The development of osmotic fragility—representing loss of tensile strength of the cell-wall—was measured by the degree of lysis of the organisms (depression of light scattering) when pipetted into a buffered medium of low osmotic pressure (0·01 *M* phosphate buffer *p*H 6·8) compared with equivalent samples pipetted into *M* sodium chloride containing the same buffer. Rapid development of osmotic fragility without appreciable lysis of the 'protoplasts' occurs at 25° in 0·3 *M* sodium malonate in 0·5 molal L-arabinose at neutral *p*H. The rate of 'protoplast' release is greater the faster the growth of the organisms at harvesting; and, for exponential phase growth in an aerated 3 per cent tryptone, 1 per cent glucose, 0·1 per cent 'Marmite' medium at 25°, half the organisms become osmotically fragile in less than 60 min.

Anoptral contrast microscopy (Messrs. Reichert, Austria) shows that the organisms are initially strongly plasmolysed in the autolysis medium (Fig. 1*a*). The chains of organisms become shorter as autolysis proceeds; but when complete osmotic fragility is achieved the organisms are still cylindrical. Transformation to spheres commences some hours later (Fig. 1*b*) and nears completion in about 12 hr. Similar results have been obtained with *Aerobacter aerogenes* although sphering is much more sluggish in this organism. It is possible that the plasma-membrane and/or protoplasm of these organisms normally possess enough mechanical rigidity to resist the tendency to assume a spherical shape even when the cell-wall has been lost or has ceased to possess mechanical rigidity.

We are indebted to Mr. R. A. Fox for photography, and to the Scottish Hospital Endowments Research Trust for grants in aid of this work.

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Application of Large Volumes in Small Spots on Paper Chromatogram Strips

Several devices have been designed for continuous application of large volumes up to 5 ml. on chromatogram strips[1,2]. The diameter of the spots thus obtained is usually 1 cm. or more, and considerable time is needed.

In order to apply relatively large volumes in very small spots on narrow paper strips in a reasonably short time, the following apparatus was constructed, in which a strong centripetal stream of warm air is concentrated around the place of application on both sides of the paper.

The apparatus is made of glass and consists of two parts (Fig. 1).

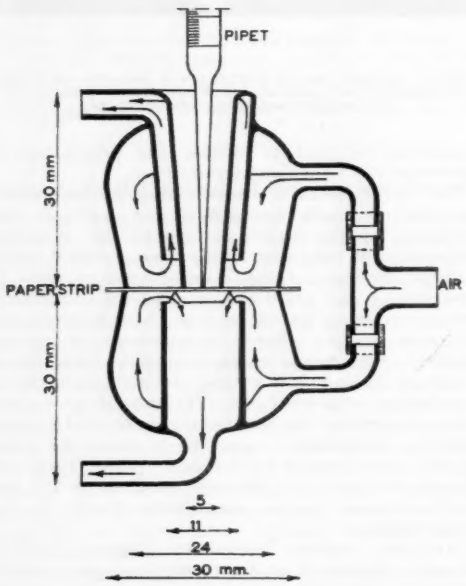

Fig. 1

The upper part is made of three concentric tubes, of diameters as indicated, fused together at the top. The middle tube is 2 mm. shorter than the other two, which have been ground down afterwards so as to end at exactly the same level. An air inlet is fused to the outer tube, the outlet is between the middle and the innermost tube.

The lower part is made symmetrical with the upper part, but without the innermost tube. The inner tube is again shorter than the outer one by 2 mm. and provided with four small points, the ends of which have been made level with the rim of the outer tube by grinding.

The paper is firmly held in its place by the rims of the two outer tubes of the innermost tube of the upper part, and the points of the inner tube of the lower part. The two parts are held together by slightly flexible rubber joints on the air inlet.

In this way even very narrow chromatogram strips 6 mm. wide can be used, when a paper mask is inserted. The tip of the applying burette or pipette is put on to the paper by entering it into the innermost tube of the upper part, and is protected by it from the air stream.

Air is blown through the apparatus from the compressed-air main after passing a filter and a heated copper spiral. A thermometer permits control of temperature.

The solution can be applied by means of a microburette of the Scholander or Rehberg–Kirk[3] type or by means of an Agla microsyringe. Thus outflow of solution, air stream and air temperature can all be controlled.

The time needed for application depends on the paper, the temperature used, and the volatility of the solvent. With various sorts of paper and solvents very small spots can be obtained in a reasonably short time: dilute solutions can be applied in a spot of 4–5 mm. diameter at a rate of 0·1 ml. in less than 10 min. for water, and less than 5 min. for butanol at 50° C. It is more convenient to condense volumes larger than 1 ml. by evaporation before application.

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Chromatography of Insulin on Calcium Phosphate Columns

Swingle and Tiselius[1] investigated the behaviour of the protein phycoerythrin when subjected to chromatography on columns packed with hydrated tricalcium phosphate supported on kieselguhr. It was found that the protein could be displaced by low concentrations of phosphate buffer. In a further study by Tiselius[2] it was found that other proteins could be displaced to give sharp elution zones when using aqueous solutions containing sodium phosphate.

The purpose of this communication is to record some results obtained when solutions of insulin stored under various conditions were subjected to chromatography on calcium phosphate–kieselguhr filled columns, eluting with sodium phosphate buffer of linearly increasing concentration.

The method used for the preparation of the calcium phosphate gel was essentially that of Keilin and Hartree[3], and each column contained 40 ml. gel supported on 26 gm. kieselguhr. The insulin was adsorbed at low ionic strength and eluted with the phosphate gradient increasing from zero to 0·05 *M* (*p*H 7·3) over a volume of 150 ml.; the concentration was then maintained at 0·05 *M*. The eluting solvent contained 0·5 per cent sodium chloride. Fractions of 3·5 ml. volume were collected and the optical density of each fraction at 276 mμ determined on a Unicam *SP* 500 instrument.

When the insulin solution was freshly prepared, the protein was eluted as a reasonably sharp peak (insulin 1) showing evidence of tailing. Any preservative such as phenol was only slightly, if at all, adsorbed and was eluted as a band ahead of the insulin. When the insulin solution was stored for a period of time in acid solution before subjecting to chromatography, it was found that a fraction of the insulin was transformed to a modification (insulin 2) which was eluted behind the band originally observed. On increasing the period of storage, the fraction of insulin changed increased still further. This effect is illustrated by

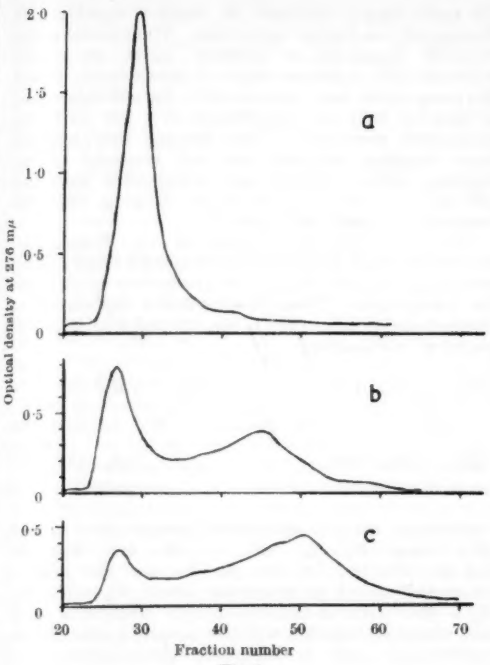

Fig. 1

the accompanying elution curves (Fig. 1), for insulin solution freshly prepared (*a*), and when stored for four days (*b*) and eight days (*c*), at 40° C. and *p*H 3·0.

Insulins 1 and 2 were isolated after elution and subjected again to chromatography, when it was found that each gave its appropriate peak on the elution curves. Bio-assay of materials isolated from the two peaks indicated that insulin 2 retained most, if not all, of the original potency in spite of the marked difference in chromatographic behaviour. A mouse assay gave the ratio of the potency of insulin 2 to insulin 1 as 0·92 ($p = 0·95$, limits 0·827 and 1·03).

It was found that the decrease in concentration of unchanged insulin, as represented by the area under the first insulin peak of the elution curve, followed first-order kinetics, at least for the early stages. Experimental values obtained for the half-life for the transformation of insulin 1 to insulin 2 at *p*H 3·0 and various temperatures are given in Table 1.

These values correspond to an energy of activation of 25,000 cal./mole. The rate of reaction is increased by lowering the *p*H and decreased by increasing the *p*H of the solution for storage. It appears to be affected only slightly, if at all, by sodium chloride concentration, by increasing the zinc concentration, or by removing the zinc from the insulin.

Preliminary results from Dr. Johnson and Mr. Rowe, of the Department of Colloid Science, Cambridge, who are investigating the two fractions, have indicated that a molecular-weight change may be associated with the transformation of insulin 1 to insulin 2.

Table 1

Storage temperature (° C.)	Half-life
0–4	3·0 years
30	14·8 days
40	3·84 days
50	1·11 days
60	10·6 hours

Further work is in progress on this effect, and it is hoped to publish detailed results in due course. I wish to thank Mr. W. Brown for assistance with the experimental work, Mr. K. L. Smith for the bio-assay, and the directors of Boots Pure Drug Co., Ltd., for permission to publish this communication.

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An Improved Method for the Preparation of Sialic Acid or Acetylneuraminic Acid

Although two decades have passed since the discovery of sialic acid by Blix[1], few investigations on this acid have been reported, due possibly to the difficulty of the preparation of the acid and the small yield. Recently Odin[2] reported a modified method for the preparation of sialic acid by mild acid hydrolysis in good yield instead of the old method, in which 'water hydrolysis' was employed. I have found that sialic acid is almost quantitatively adsorbed on activated charcoal, and this provides a convenient method for its preparation in good yield.

30 gm. of bovine submaxillary mucin were heated in 30 ml. of distilled water in a sealed tube for 2 hr. at 100° C. After cooling, the solution was dialysed against distilled water for 20–24 hr., changing the water three times during dialysis. The dialysate showed not only a positive direct Ehrlich reaction and Fehling test, but also the biuret reaction. However, the Molisch reaction was negative. The combined dialysate was concentrated *in vacuo* to about 50 ml. The solution became slightly pink during the concentration. The concentrated solution was then passed through an activated charcoal (about 150 mesh) column (2 cm. × 10 cm.). The effluent solution was colourless and was negative in the direct Ehrlich reaction. Thus sialic acid had been quantitatively adsorbed on charcoal. The column was washed with 100–150 ml. of water, and no sialic acid was lost from the column. After removal of the washing water, sialic acid was eluted with 180 ml. of 98–99 per cent methanol. Sialic acid was scarcely eluted at all with ethanol. The effluent solution was evaporated *in vacuo* to dryness. The residue, which did not show the biuret reaction, was dissolved in dry methanol and filtered into a centrifuging tube, and dry ether was carefully added to the filtrate, producing a flocculent precipitate. When no more flocculent precipitate occurred on adding ether, the precipitate was centrifuged off. The volume of ether needed did not exceed that of the methanol solution. Dry petroleum ether (about 5 ml.) was added dropwise to the clear colourless supernatant solution, whereupon the solution became turbid. On allowing to stand in an ice-box, crystalline sialic acid appeared on the glass wall. The form of the crystal was similar to that reported by Blix[1], and the yield was about 350 mgm. from 30 gm. of the mucin. The nitrogen

content was 4·1 per cent; the same value was obtained for every preparation. Other chemical properties of the crystal were identical with those of bovine sialic acid described by Blix. The specific rotation of the crystal, however, was different from that of bovine sialic acid reported by Blix: according to Blix[3] bovine sialic acid has the value of $[\alpha]_D^{22} = +8 \pm 2°$; whereas my sample showed $[\alpha]_D^{20} = -42{\cdot}0°$ (in water) after 10 min. and $-32{\cdot}8°$ after 30 min. The value of the specific rotation extrapolated to zero time was $-50°$. Thus mutarotation was observed with the substance. This evidence accords with the assumption of the presence of a potential aldehyde group in sialic acid[4,5].

From the optical rotation and nitrogen content of the product I have obtained it seems to be identical with Klenk's acetylneuraminic acid[6] and sheep sialic acid[3]. Recently, Klenk *et al.*[7] stated that acetylneuraminic acid should be identical with sheep sialic acid. Whether the product I have obtained is natural bovine sialic acid or not is not yet certain. It may be a slightly decomposed bovine sialic acid. Although bovine sialic acid was distinguished from neuraminic acid by the aid of colour reaction[5], Blix's authentic bovine sialic acid (kindly provided by Prof. Blix) could not be distinguished from my product by colour reaction.

The details of this investigation will appear elsewhere; further experiments are now in progress.

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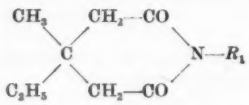
New Analeptics and Hypnotics related to the Barbiturate Antagonist, 'Bemegride'

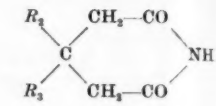
The preparation of various glutarimides in these laboratories for testing as possible analgesics led to the discovery[1] in the Department of Pharmacology and Physiology, University of Melbourne, of the antibarbiturate activity of ββ methyl ethyl glutarimide ('Bemegride', 'Megimide'), from which a new method of treatment for barbiturate intoxication has been developed[2]. This prompted the investigation of related β-substituted glutarimides and derivatives of 'Bemegride' for similar activity. A series of compounds was therefore synthesized for examination, and the results of preliminary pharmacological trials are reported here.

The effects of the test compounds on the sleeping times induced by pentobarbital sodium in mice were compared with that of 'Bemegride', using groups of ten mice. The control group received 60 mgm./kgm. pentobarbital sodium. The test group received pentobarbital sodium (60 mgm./kgm.) and the test compound (25 or 50 mgm./kgm.), followed by further injections of the test compound at the same dosage at 15 min. intervals. The third group received pentobarbital sodium (60 mgm./kgm.) and 'Bemegride' (25 mgm./kgm.), followed by further injections of 'Bemegride' as for the test group. The control group received injections of distilled water at similar intervals. All injections were intraperitoneal. Where the compounds were too insoluble for administration in aqueous solution, suspensions in 1 per cent gum tragacanth were used. The sleeping time was the time elapsing between loss and recovery of the righting reflex. Where any appreciable reduction (50 per cent or more) in mean sleeping time was observed, a *t*-test was applied.

The two hydrolysis products of 'Bemegride', ββ methyl ethyl glutaramic acid and ββ methyl ethyl glutaric acid, were found to be ineffective as barbiturate antagonists. Three N-substituted derivatives of 'Bemegride' (I where R_1 = Me, Et and Ph) were also found to be inactive.



(I)



(II)

Fourteen other β-substituted glutarimides of type (II), where R_2, R_3 = H, H; Me, H; Me, Ph; Et, H; Ph, H; Et, Et; Pr, Pr, and the series of ββ methyl alkyl glutarimides, where R_2 = Me and R_3 = Me, *n*-Pr, *n*-butyl, *i*-butyl, *n*-amyl, *n*-hexyl and *n*-heptyl, together with the β spiro cyclopentane, cyclohexane and cycloheptane glutarimides, were then examined for analeptic activity.

Three compounds, the β spiro cyclopentane, ββ methyl *n*-propyl and ββ diethyl glutarimides, were found to have similar analeptic effect to that of 'Bemegride', the relative activities being in the order named. The cyclopentane compound was almost as effective as 'Bemegride' at the same dose-level (25 mgm./kgm.) in producing a 50 per cent reduction in sleeping time, while the other two produced the same result when administered at 50 mgm./kgm. (*t*-tests gave $P < 0{\cdot}01$ in all cases). Like 'Bemegride', all three caused convulsions in mice when injected alone at doses of 15–50 mgm./kgm., the cyclopentane and diethyl compounds being lethal at 20 and 75 mgm./kgm. respectively. The methyl *n*-propyl compound is less toxic and at doses up to 400 mgm./kgm., induced periodic convulsions for upwards of one hour, when the animals usually recovered.

The β ethyl, ββ methyl *iso*butyl and the other two β spiro cycloalkane glutarimides were also convulsants when administered alone at 20–50 mgm./kgm. Treatment of the animals with pentobarbital before injection of any of these compounds prevented convulsions in all cases; but the sleeping times were not affected.

ββ Methyl *n*-butyl glutarimide was found to have hypnotic effects in mice, its action being opposite to that of the convulsant methyl *iso*butyl compound. The methyl *n*-amyl and methyl *n*-hexyl glutarimides were also found to have hypnotic activities, while the methyl *n*-heptyl compound had no apparent pharmacological action.

These three hypnotic glutarimides, being rather insoluble in water, were administered as suspensions in 1 per cent gum tragacanth. For all three compounds, the minimum hypnotic dose is 150–200 mgm./kgm. and the approximate *LD*50 is 600 mgm./kgm. Using groups of ten female albino mice, the mean sleeping times induced by each compound at a dose

Table 1

-glutarimide	Dose level (mgm./kgm.)	No. losing righting reflex	Mean induction time (min.)	Sleeping time (min.) Mean ± S.E.
ββ Methyl n-butyl-	200	7	7	3·5 ± 1·23
	300	10	6	23·1 ± 2·75
ββ Methyl n-amyl-	200	10	5	42·3 ± 6·02
ββ Methyl n-hexyl-	200	10	9	17·0 ± 2·62

of 200 mgm./kgm. were obtained, and are listed in Table 1.

The methyl *n*-amyl compound thus appears to be the most effective of the three. No signs of toxic effects were observed at these doses. Sleeping times up to 5 hr. were induced with all three hypnotics at doses of 400–500 mgm./kgm.

Finally, it has been shown, by the procedure used for screening the other test compounds, that the hypnotic action of these three glutarimides is very effectively antagonized by the methyl ethyl glutarimide, 'Bemegride'. Of a group of ten mice injected with 200 mgm./kgm. of the methyl *n*-amyl compound followed by a single injection of 20 mgm./kgm. 'Bemegride', five did not lose the righting reflex at all, and the mean sleeping time of the remaining five was reduced to less than one-third the control value. No convulsions were observed, indicating a swift antagonism between the two glutarimides in the animals.

From the pharmacological results so far obtained the following conclusions regarding the activity of 'Bemegride' as a barbiturate antagonist are evident. (1) The intact glutarimide ring is essential for analeptic effect, as the two hydrolysis products have no activity. (2) The inactivities of the *N*-substituted derivatives of 'Bemegride' demonstrate the importance of the imido hydrogen atom. (3) 'Bemegride' is not unique among β-substituted glutarimides as a barbiturate antagonist, as three closely related compounds have been shown to have similar activities.

In the series of β methyl β *n*-alkyl glutarimides, which contains two analeptic compounds, 'Bemegride' and ββ methyl *n*-propyl glutarimide, further extension of the *n*-alkyl substituent to butyl, amyl and hexyl results in hypnotic activities in these three compounds. 'Bemegride' effectively antagonizes the hypnotic effect in mice of these glutarimides. The methyl *n*-heptyl glutarimide, however, has no particular activity.

Work is continuing on compounds of the glutarimide type, and further pharmacological results, together with complete chemical information, will be published shortly.

I should like to thank Prof. F. H. Shaw, of the Pharmacology Department, University of Melbourne, who allowed me to use the facilities of that Department for some of the earlier testing, and also the directors of Nicholas Proprietary, Ltd., for permission to publish this communication.

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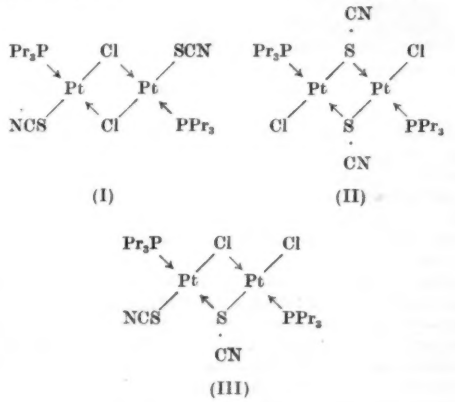
Use of the Infra-Red Spectrum to distinguish Bridging from Terminal Thiocyanato-S-Groups in Co-ordination Compounds

In 1952 the existence of two thiocyanato-complexes of composition $(PPr^n_3)_2Pt_2Cl_2(SCN)_2$ was reported[1]. The labile α-isomer had m.p. 144°–152° and the stable β-isomer, m.p. 173°–174·5°. These isomers have dipole moments of less than 2 Debye units and so must have the tri-*n*-propylphosphine groups in *trans*-positions to each other. Possible structures are (I), (II) and (III).



A substance of structure (II) might also exist in two geometrically isomeric forms, according to whether the CN groups are in *cis* or in *trans* relationship to each other about the planar PtS_2Pt ring. Since such geometrical isomerism, arising from the aplanarity of the valencies from the 3-covalent sulphur atoms, was then unknown, it was considered that the α- and β-isomers would most probably be structural isomers, and from general considerations of their relative stabilities they were assigned structures (I) and (II) respectively. At that time no means of confirming or disproving that assignment of structures was available to us; but now using infra-red methods we conclude that both isomers have their SCN groups in bridging positions, and so cannot be the structural isomers at first postulated.

We find that the infra-red spectrum affords an excellent method of determining whether thiocyanato-S groups are in terminal or in bridging positions. This conclusion is based on the examination of a number of thiocyanato-complexes of platinum (II) and of palladium (II). The spectra were obtained from paraffin oil mulls of the powdered crystalline complexes using a Grubb-Parsons *S3A* spectrometer fitted with a lithium fluoride prism. The observed frequencies (to the nearest $cm.^{-1}$) are listed in Table 1. All the thiocyanato-complexes which we have studied exhibit at least one strong absorption band in the region of 2,100–2,170 $cm.^{-1}$, and this can be unequivocally assigned to the SCN stretching modes. The particular modes are presumably derived[2] from ν_3 of SCN^-, which has[2] a frequency of 2,066 $cm.^{-1}$. All the mononuclear complexes have an absorption band in the range 2,100–2,120 $cm.^{-1}$, and those binuclear complexes which from their composition must contain both bridging and terminal SCN groups have additional bands in the range 2,150–2,182 $cm.^{-1}$. It is evident that bridging SCN groups give rise to

Table 1. Strong Absorption Bands in the 4μ Region of the Spectra of some Thiocyanato-Complexes of Platinum and Palladium

Compound	Bridging SCN	Terminal SCN
$(AsPr^n_3)_2Pd(SCN)_2$	—	2,115
$(AsBu^n_3)_2Pd(SCN)_2$	—	2,113
dipy Pd(SCN)$_2$*	—	2,100
$(PBu^n_3)_2Pd(SCN)_2$	—	2,110
$(PPr^n_3)_2Pt(SCN)_2$	—	2,120
$(AsPr^n_3)_2Pd_2(SCN)_4$	2,154	2,120
$(PBu^n_3)_2Pd_2(SCN)_4$	2,162	2,120
$(AsBu^n_3)_2Pt_2(SCN)_4$	2,153	2,120
$(PPr^n_3)_2Pt_2(SCN)_4$	2,182, 2,166	2,105
$(AsPr^n_3)_2Pd_2(SCN)_2Cl_2$	2,154	—
$(AsBu^n_3)_2Pd_2(SCN)_2Cl_2$	2,154	—
$(PBu^n_3)_2Pd_2(SCN)_2Cl_2$	2,159	—
α-$(PPr^n_3)_2Pt_2(SCN)_2Cl_2$	2,162	—
β-$(PPr^n_3)_2Pt_2(SCN)_2Cl_2$	2,160	—

* *Dipy = 2 : 2′-dipyridyl*

stretching frequencies about 30–80 cm.$^{-1}$ higher than the corresponding frequencies originating from terminal SCN groups, and that all the complexes of the type $L_2M_2(SCN)_2Cl_2$ (L = $AsAlk_3$ or $PAlk_3$; M = Pd or Pt) which we have investigated have both their thiocyanato-groups bridging the two metal atoms.

This conclusion rules out the original proposal that the α- and β-forms of $(PPr^n_3)_2Pt_2Cl_2(SCN)_2$ are the structural isomers (I) and (II) and points to both having the structure (II). On this basis the two isomers can only be accommodated if they are the geometrical isomers discussed above, and would provide the first example of such isomerism. Against this it can be argued that all SCN stretching modes of the *cis*-form of (II) should be infra-red active and hence its spectrum should have two bands in the neighbourhood of 2,160 cm.$^{-1}$, whereas we observe only one. However, in complexes containing heavy metal atoms accidental degeneracies may easily occur and prediction from group theory concerning the numbers of bands which should occur in the infra-red spectrum can be misleading. As evidence for this we have the single absorption band in the spectrum of the dipyridyl complex which cannot be centrosymmetrical. It is proposed to investigate these points more fully.

The difference between the SCN stretching frequencies of the bridging and terminal groups is in the sense to be expected if it were caused by electronic effects. The valence force treatment of the SCN^- ion given by Penney and Sutherland[2] indicates that the frequency of the 4μ band is determined to a large extent by the CN bond-stretching force constant. The CN bond order will increase with increasing positive charge on the sulphur atom, and so the frequency of the 4μ band should be greater when the sulphur atom is co-ordinated to two metal atoms than when it is only co-ordinated to one, as we observe.

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Vapour Pressures of Some Disperse Dyes

The vapour pressure, heat and standard entropy of sublimation of two disperse dyes, 1-methylaminoanthraquinone and 1-(β-hydroxyethyl)aminoanthraquinone, have been determined.

Vapour pressures of the former were determined over the temperature range 110°–130° C., and of the latter over the range 150°–165° C., by a modification[1,2] of Knudsen's effusion method. The vapour effused through a hole of known area into a hard vacuum and was condensed on a cold finger. The rate of effusion was measured by observing, by means of a cathetometer, the deflexion of a silica spring from which was suspended the effusion vessel. This vessel had been previously calibrated at approximately 40° C. by using benzophenone, the vapour pressure of which has been accurately determined by Neumann[3]. As a check, a second vessel containing a hole of smaller area was also used, and the results agreed within the experimental error. The method assumes that the effusing vapour is monomolecular.

The dyes were purified by chromatography and sublimation *in vacuo*. Spectrographic analysis of material sublimed in the temperature ranges, as above, shows that no decomposition of the material takes place under these conditions.

On plotting $\log_{10}p$ (cm. of mercury) against $10^3/T$, where T is the absolute temperature, the results were found to fit the equation

$$\log_{10}p = \frac{a}{T} + b$$

Data for the two dyes are given in Tables 1 and 2.

Table 1

	a	b
1-Methylaminoanthraquinone	−6,740	13·435 (±0·036)
1-(β-Hydroxyethyl)aminoanthraquinone	−7,973	14·819 (±0·005)

Table 2

	1-Methylaminoanthraquinone	1-(β-Hydroxyethyl)-aminoanthraquinone
Heat of sublimation (kcal. mole^{-1})	30·85	36·50
Standard entropy of vaporization for vapour at one atmosphere (cal. mole^{-1} deg.$^{-1}$)	52·87 (±0·30)	59·24 (±0·01)

Majury[4] has shown that, in the case of five 'model' dyes, namely, *p*-nitroaniline, NN-dimethyl-*p*-nitroaniline, azobenzene, *p*-aminoazobenzene, and NN-dimethyl-*p*-aminoazobenzene, from a knowledge of vapour pressures and dyeing adsorption isotherms from the vapour phase, the absolute heat of association of the model compound with the substrate can be found.

In the present work, the compounds used are actual dyestuffs with much smaller vapour pressures, and it is hoped, eventually, to correlate these results with data on the energy and entropy of adsorption of the

dye vapour on suitable substrates, and with data on the diffusion of dyes in such media.

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Oxidation-Reduction Reactions of Metal Salts in Non-aqueous Solvents

The recent exploitation of electron exchange reactions in aqueous solutions[1] has provided valuable information on oxidation-reduction reactions in general and stimulated their study. The situation for the latter reactions in non-aqueous solvents is completely different, little being known about them despite their importance in trace-metal catalysed autoxidations[2]. Collinson and Dainton[3] have pointed out that radicals produced during polymerization will react with a variety of metal salts in a number of media. Useful comparative data can also be obtained by studying the reactions of metal salts with a stable free radical. In this instance the reactions between metal acetates and the radical αα′-diphenyl-β-picrylhydrazil have been investigated. First-order kinetics for each reactant were observed; below are listed specific rate constants for reactions in anhydrous acetic acid at 25° C.

Metal acetate	Specific rate constant (M^{-1} sec.$^{-1}$)
Lead (IV)	35
Cobalt (III)	22
Cerium (IV)	55
Iron (III)	88

Other acetates, namely, those of chromium (III), copper (II) and manganese (III), also react with the free radical, but kinetic data are not available yet. In all these reactions the rate was reduced by the addition of methyl alcohol or benzene but increased markedly by the addition of water.

Further interesting reactions were found to occur between valence states of metal acetates; again, anhydrous acetic acid was the main solvent used. The systems which were examined in detail are lead (IV)–cobalt (II), lead (IV)–cerium (III) and lead (IV)–manganese (II); first-order dependence on all the reactants except manganous acetate was observed. Below is a table of apparent activation energies and specific rate constants for these systems.

	Specific rate constants (M^{-1} sec.$^{-1}$)	Activation energies (kcal./mole)
Lead (IV) + cobalt (II)	0·56	14 ± 1
Lead (IV) + cerium (III)	0·24	21 ± 1
Lead (IV) + manganese (II)	0·43	14 ± 1

Attempts are being made to identify the reacting species by noting the effect of the addition of other solvents and unreactive salts on the reaction-rates, absorption spectra and ion migrations with an applied potential. For example, in the lead (IV)–cobalt (II) reaction addition of water retarded the reaction-rate whereas sodium acetate accelerated it; both these additives affected the absorption spectrum of cobaltous acetate markedly; with added water, migration to the cathode only was observed, but when sodium acetate was present instead, migration to both anode and cathode occurred.

Preliminary work has shown that reactions between the valence states of the acetates of chromium, copper, mercury and iron also take place in dry acetic acid. In addition, chromous acetate may be oxidized to the chromic state in methyl alcohol by some metal acetates.

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Crystal Structure of 1 : 2-Benzanthracene

As part of an investigation into Daudel and Pullman's theory[1,2] concerning the connexion between carcinogenic activity and the chemical structure of benzanthracene derivatives, we have made a detailed study of the crystal structure of 1 : 2-benzanthracene.

Crystal studies of this substance have been reported previously by Iball[3], who, however, appears to have obtained a *c*-crystal axis dimension which is twice the length we have found.

As already reported by Iball, 1 : 2-benzanthracene is very difficult to obtain in crystals suitable for single-crystal analysis. We have found that a dilute solution of benzanthracene in a mixture of 1/3 methanol to 2/3 ethanol, which is allowed to evaporate slowly (24 hr.) at room temperature, will deposit perfect, but very small, crystals (0·1 mm. × 0·3 mm. × 0·5 mm.). Slowing down the rate of evaporation did indeed enable one to obtain larger crystals, but single-crystal photographs of these invariably showed them to be twins.

We have carried out a three-dimensional Fourier analysis of 1 : 2-benzanthracene in order to measure

Table 1. Old and New Crystal Data of 1 : 2-Benzanthracene

Monoclinic (A.)	*a*	*b*	*c*	β	*Z*	Space group
Iball	7·91	6·43	23·96	99°	4	C_{2h}^5–$P2_1/m$ or C_2^2–$P2_1$
	7·95	6·50	12·12	100·5°	2	C_2^2–$P2_1$

Table 2. Atomic Co-ordinates of the 18 Carbon Atoms in Thousandths of a Unit-Cell Edge

Atom	*x*	*y*	*z*
A	119·0	−53·3	370·1
B	188·5	7·3	489·2
C	164·7	−134·4	576·0
D	214·1	−70·2	681·6
E	287·3	111·8	720·9
F	327·5	130·7	845·0
G	414·7	324·0	876·1
H	451·2	467·2	796·2
I	409·1	432·0	680·7
J	328·8	261·7	643·4
K	279·2	208·0	512·6
L	302·5	338·9	436·2
M	234·9	292·5	324·9
N	263·6	462·6	241·2
O	195·1	414·3	131·8
P	115·7	232·6	105·7
Q	90·1	98·8	176·1
R	153·8	104·9	287·6

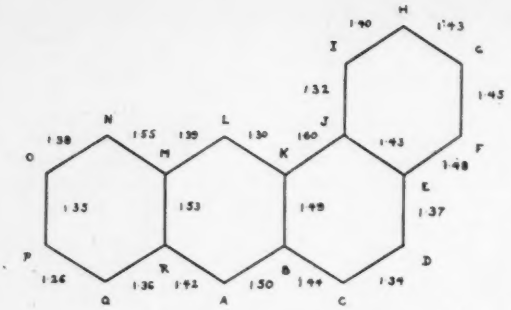

Fig. 1

the bond-lengths and electron densities of the *K*-region, so named by Daudel and Pullman[1].

Because of the lack of a centre of symmetry in three dimensions, the total absence of atomic resolution in the only centrosymmetric projection (*h0l*), and the low percentage of measured reflexions (518 out of a permitted total of 1,658), the refinement of the structure has been difficult and is not yet complete. For this reason the bond-lengths (in A.) shown in Fig. 1 are only tentative. To date, the refinement has consisted of three rounds of three-dimensional Fourier refinement (for which our thanks are due to Prof. R. Pepinsky, who very kindly allowed us to use *X-RAC*) and nine rounds of three-dimensional least-squares refinement carried out on the *IBM* 701 computer and Remington Rand's *UNIVAC*. The structure now has a discrepancy *R* of 21·5 per cent over the 518 planes. The molecule is planar within experimental error. Further work is in progress to improve the discrepancy, and full details will be reported later.

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Absorption of Oxygen and Carbon Monoxide by Barium Alloy Getters

Wagener[1] has described a novel method of finding both the pumping speed and capacity of getters, and has made measurements[2,3] with common gases and barium alloy getters of the type used in radio valves. The results obtained were conflicting. In the earlier paper[2] it was reported that the speed of pumping depended upon the amount of ionizing electron current in a nearby diode or ionization gauge. Wagener's measurements were made in a range of electron current from 5 m.amp. to 20 m.amp. If these measurements are extrapolated to zero current they show that the speed of pumping is not then zero, contrary to the hypothesis suggested in the paper. In the later publication[3] it was reported that the speed of pumping was about the same without, as with, an ionizing electron discharge. The present work was undertaken to decide between these contrary findings. It was decided to study the pumping of oxygen, because the chemical affinity of barium for this gas would make more remarkable any necessity for electron current.

The apparatus used here was similar to that described by Wagener[1-3], except that, for measuring pressures without using any ionizing electron current, a Pirani gauge was fitted. In addition, pressure measurements could be made with the ionization gauge over a range of electron current, from less than 1 microamp. to more than 1 milliamp. During most of the present experiments, the pressure above the getter was of the order 10^{-6} mm. mercury. The barium alloy getters used were of the *KIC* type, 20 mgm. size, with a non-magnetic stirrup, as in television tubes.

It was found that the speed of pumping of oxygen by a barium getter film was very little changed when an ionizing (180 V.) electron current was run nearby. A typical set of values of speed and current was as follows:

Electron current (μamp.)	0	1	5	10	50	100	500	1,000
Speed of pumping (l.sec.$^{-1}$)	1·50	1·50	1·50	1·50	1·52	1·54	1·67	1·85

The slight variation of speed with current was linear. Thus barium getters pump oxygen in the absence of any ionization.

The speed of pumping of the getters was found to vary with time, as had already been reported by Wagener[2]. The variation of the speed of pumping with time and temperature is shown in Fig. 1. The increase of speed with temperature should be noted. Moreover, the amount of oxygen taken up by the getter (capacity) increased with temperature. At room temperature the capacity was independent of the thickness of the getter film deposited, so that thick films were still opaque and metallic-looking when pumping ceased. At higher temperatures the capacity increased with the thickness of the film, and the deposit became translucent at the end of pumping. These results show that the mechanism of gettering involves diffusion.

In spite of ionization not being necessary for the pumping of oxygen by barium, it was suspected that the hot filament in an ionization gauge might influence the speed of pumping. The measurements of the variation of the speed of pumping of oxygen, with electron current, were made with the getter film at room temperature, while the speed was not changing with time. However, it was found, from Pirani gauge measurements, that during the falling-speed period, towards the end of the life of a getter film, all pumping ceased if an incandescent tungsten filament near the getter was switched off. The tungsten filament became effective when its temperature was raised above 1,800° K.; but increasing the temperature to 2,100° K. did not increase the speed further. Moreover, the speed was not raised further by increasing the number of filaments that were heated. Thus, some product of the interaction of oxygen molecules with an incandescent tungsten filament, probably atomic oxygen, has a catalytic effect upon the taking up of oxygen by a failing barium getter film.

A considerable increase of speed of pumping and of capacity with temperature was also found in experi-

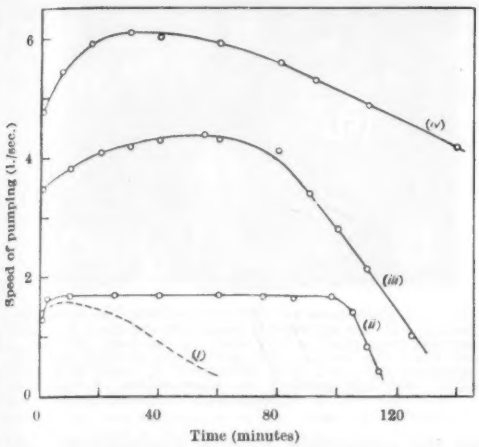

Fig. 1. Variation with time and temperature of the speed of pumping of oxygen by barium. Curve (i) represents Wagener's work, with an area of 12 sq. cm. at an unknown temperature. The present work is with an area of 8 sq. cm. at the following temperatures: (ii) room temperature; (iii) 40° C.; (iv) 70° C.

ments with carbon monoxide. This result contrasts with the small increase reported by Morrison and Zetterstrom[4]. The increased capacity was marked by the getter film becoming translucent, although stained brown.

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Change in Surface Area of Anthracite on Heat Treatment

Maggs[1] and Malherbe[2], among others, have shown that coal behaves as a molecular sieve material. That is, the adsorption of nitrogen and argon at 77° K. is restricted because of activated diffusion into pores of molecular dimensions and gives data only on the readily accessible macropore area of coal. From heats of wetting and gas-adsorption data at higher temperatures, the macropore area is shown to represent an insignificant part of the total surface area of most coals.

The presence of a large micropore area in coal affects many of its properties. One property which is thought to be markedly affected is the thermal stability of anthracite on pyrolysis. Raw anthracite when used as a metallurgical fuel is susceptible to thermal shock, usually resulting in the lowering of its physical strength and subsequent size degradation. This phenomenon is thought to be primarily caused by the large increase in gas pressure in the micropores produced by the difficulty of releasing volatile matter from these pores upon heat treatment. It is with this thought in mind that a comprehensive programme has been initiated to study the nature of the micropore surface area in anthracites, its change with heat treatment, and its relation to decrepitation. An initial result of interest is being reported at this time.

The anthracite studied has the following proximate analysis on the as-received basis: water, 3·4 per cent; volatile material, 2·9 per cent; ash, 7·1 per cent; free carbon, 86·6 per cent; and sulphur, 0·54 per cent. Adsorption studies were performed on minus-60 mesh samples (Tyler series) of raw and calcined anthracite. Calcination was conducted in a reducing atmosphere with samples heated to 1,200° C. in two hours and maintained at this temperature for two additional hours. Surface areas of the anthracite were determined from nitrogen adsorption at 77·2° K. and carbon dioxide adsorption at 194·6° K. using the procedure and Brunauer–Emmett–Teller equation discussed by Emmett[3]. Final adsorption pressures were read after 30 min. even though equilibrium was not completely attained.

Table 1 presents the surface area data. The nitrogen value can be considered essentially the macropore area, whereas the carbon dioxide value can be considered essentially the total area. The nitrogen value would be expected to consist of some micropore area, and the carbon dioxide value would be expected to be somewhat less than the total area since equilibrium was not reached. Naturally, any arbitrary adsorption time of reasonable duration has the above limitations, and this fact must be kept in mind when interpreting the data. It should also be pointed out that good agreement of surface areas from nitrogen and carbon dioxide adsorption on carbons known to have an insignificant microporosity has been obtained[4].

Table 1. Surface Area of Raw and Calcined Anthracite

Treatment	N_2 area, m.²/gm.	CO_2 area, m.²/gm.
Raw	11·2	175
Calcined	0·78	2·8

It is seen that for the raw anthracite the micropore area represents at least 93 per cent of the total area, whereas for the calcined material only somewhat more than 72 per cent need be in micropores. Of greater significance is the marked decrease in the magnitude of micropore area upon calcination. At least 98 per cent of the micropore area has been destroyed or blocked from access to the exterior surface on calcination at 1,200° C.

Calcination of the anthracite produced approximately a 15 per cent volume-shrinkage. In the light of the area results, it appears that this shrinkage parallels the removal of the majority of micropore area from the anthracite. Indeed, anthracite which has been calcined at a very low heating rate[5] shows good thermal stability when afterwards plunged rapidly into a hot zone, which is to be expected if the microporosity and occluded gases have been removed.

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The Golgi Apparatus and Secretion of Enzymes in Peptic Cells of Rabbit

In rabbits starved for 48 hr. with free access to water, the Golgi apparatus as shown by the Aoyama technique, as modified by me, is in the form of a compact reticulum lying close to the luminal pole of the nucleus (Fig. 1.1). After feeding, the Golgi reticulum expands and increases gradually in volume until it occupies the luminal part of the cytoplasm (Fig. 1.2–4). During increased secretory activity, the power of the Golgi substance to reduce silver nitrate or osmium tetroxide gradually increases; this suggests that besides the morphological changes, chemical changes occur in the Golgi substance. In the fed rabbits, argentophile secretory granules appear in the field of the Golgi apparatus, and as the latter hypertrophies the secretory granules increase in number (Fig. 1.2–3).

Most of the secretory granules are seen in close association with the Golgi substance; those which have moved away from the Golgi apparatus field are present above it in the supranuclear region which is usually free from mitochondria. The granules when secreted are argentophile; then they increase in size and loose their argentophily. Some of these argentophobic granules run together, forming larger spheres which ultimately accumulate at the luminal part of the cytoplasm.

It is worth mentioning that subsequent to feeding, the argentophile granules were observed in the cells; but after approximately two hours they were less frequently seen, and instead of them non-argentophile larger granules were observed. Some of these argentophobic granules were seen to be encircled either partly or completely by the Golgi substance (Fig. 1.4); this is well illustrated in the photomicrograph (Fig. 2), where argentophobic spheres (*Z*) lie in the claw-like prolongations of the Golgi substance; this indicates

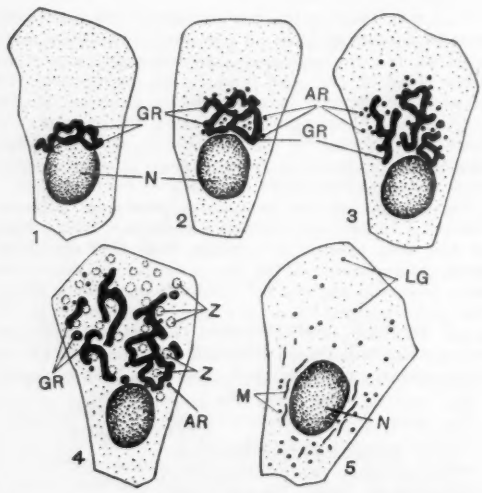

Fig. 1. 1–4 showing the morphological changes of the Golgi apparatus during the different phases of activity. 1, cell showing compact Golgi reticulum after 48 hr. fast; 2, Golgi reticulum enlarged and secretory granules appeared in its field; half an hour after feeding; 3, cell in an advanced stage of secretion; one hour after feeding; 4, cell showing the transformation of some of the argentophile secretory granules (propepsinogen) into non-argentophile pepsinogen spheres; 5, a composite cell showing lipid granules (drawn here as spheres) and mitochon ria

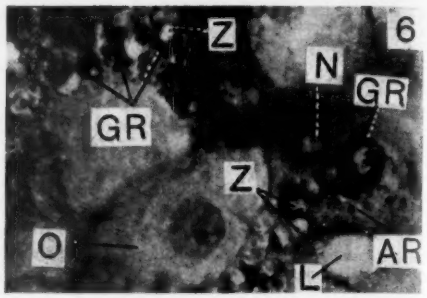

Fig. 2. A photomicrograph showing argentophile propepsinogen granules and non-argentophile pepsinogen globules which are encircled either partly or completely by the Golgi substance; two hours after feeding. *AR*, argentophile secretory granules (propepsinogen); *GR*, Golgi reticulum; *L*, lumen of gastric gland; *LG*, lipid granule; *M*, mitochondria; *N*, nucleus; *O*, oxyntic cell; *Z*, non-argentophile pepsinogen globules

that the argentophile material represents an early stage in the formation of the non-argentophile secretion granules, and that the process of transformation of young secretory granules to mature zymogen takes place in contact with the apparatus of Golgi.

In rabbits which had constant access to food the Golgi apparatus presents great variations in appearance, which indicate that the cells are in different phases of activity and that each cell appears to act as an independent unit.

I consider the argentophile granules, which appear after the intake of food, as the young or prozymogen (propepsinogen) granules; these are transformed into mature secretory granules (zymogen or pepsinogen) which are non-argentophile. None of the prozymogen or zymogen granules appears to stain vitally in neutral red, methylene blue or janus green. They have also no marked affinity for sudan dyes, and in sections prepared for the study of the mitochondria, unstained vacuoles are seen in the place of zymogen granules. The earliest secretory granules (prozymogen) are lightly stained in mitochondrial preparations; they are larger than the granular mitochondria and are restricted to the field of the Golgi apparatus.

The mitochondria are shown most clearly in material fixed in Champy's fluid and stained with Heidenhain's iron-alum hæmatoxylin or better by treating post-osmicated material for mitochondrial staining. They are present as granules, rods and filaments scattered through the cytoplasm, especially around the nucleus (Fig. 1.5). Fasting and feeding do not induce any noticeable change in the size, shape, distribution or in the number of the mitochondria.

No evidence was obtained suggesting that the mitochondria of peptic cells change into the Golgi material, secretion granules, or that they take any part in cellular secretions as claimed by some authors. On the contrary, the location of the earliest secretory granules in the Golgi apparatus field and in intimate connexion with the Golgi substance, the difference in position between the mitochondria and secretory granules, and the changes in the morphology of the Golgi apparatus during the different phases of activity seem to point to the Golgi apparatus as being the centre of enzyme formation in peptic cells. The Golgi apparatus reticulum is argentophile and osmiophile but does not stain with sudan black, neutral red or methylene blue. The apparatus seen in living

unstained or supravitally stained cells, under the phase-contrast microscope, is comparable with the Golgi apparatus picture given by silver or osmic methods.

A further account of the material is being published elsewhere.

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Relationship between Blood Concentration and Environmental Salinity in *Palaemonetes varians* (Leach)

IN Britain *Palaemonetes varians*, variety *micro-genitor*, commonly inhabits only saline water around the coastline and has never been recorded in fresh water. The prawn is, however, very abundant in water of extremely low salinity in the Cardiff area, where it occurs in the drainage ditches of farm-land adjacent to an area of salt-marsh[1]. In the summer months both the salt-marsh and the farm-land waterways swarm with larval prawns. The *P. varians* of these two regions are morphologically identical but differ physiologically, those from the latter habitat being in some way better suited for life in a low salinity environment. When in water of low salinity (such as that contained in the ditches traversing the cultivated area) they show a much smaller expenditure of metabolic energy (as measured by the respiratory rate) than those from the neighbouring, highly saline marsh pools[2].

Estimations of the osmotic pressure of blood taken from specimens of both habitats kept in different concentrations of sea-water have been measured by Baldes's modification of Hill's thermo-electric technique[3,4], in order to determine whether a difference in blood concentration exists in these two physiological races. A reduced blood concentration in a low-salinity medium would diminish the osmotic gradient and, as a consequence, decrease the amount of energy the animal would have to expend on osmoregulatory work.

The results are shown in Fig. 1. Both groups of prawns are isotonic at a salinity of about 20‰ sodium chloride in the external medium, which is in agreement with the figures given by Panikkar[5]. The blood concentrations vary slightly as the external medium changes in salinity; but these are comparatively minor fluctuations, being only about 5‰ sodium chloride over a range of 30‰ sodium chloride in the external environment. Both populations show a slight fall in the value for blood when the medium becomes diluted to a salinity below 10‰ sodium chloride. The small differences of values between the two sets of results are well within

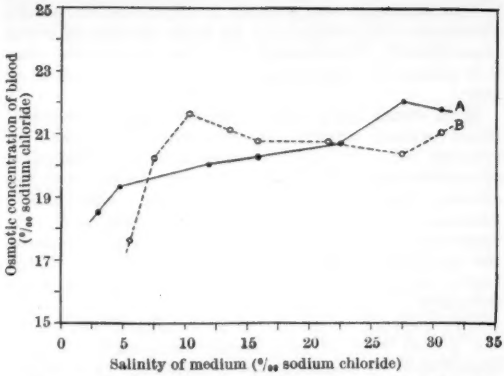

Fig. 1. Blood concentration of *Palaemonetes varians* at different environmental salinities: (*A*) salt-marsh prawns; (*B*) low-salinity prawns

the range of fluctuations due to experimental error incurred by the use of this thermo-electric technique, and shows no significant difference in their concentrations. Thus the marked difference in energy consumption in media of very low salinity, displayed by these two populations of *P. varians*, is not due to one of the groups becoming subjected to a reduction in the osmotic gradient between external environment and internal body fluid. The blood concentration is the same in both cases and both are typically homoiosmotic.

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A Spiral 'Valve' in the Hepatic Portal Vein

THE occurrence of laminar flow in the hepatic portal vein is acceptable on hydrodynamic grounds[1]. In any consideration of the probable distribution within the liver of blood from a particular tributary of the portal vein the anatomy of the vein is important. Drs. C. H. Barnett and W. Cochrane[2] suggest that the relative diameters of tributary and main vein and the angle of union are the important factors in determining the path of the streams. I have recently observed an anatomical structure in the portal vein which on theoretical grounds would appear to be more important than either of these factors.

In neoprene latex casts of the portal vein of rabbits there is a constant spiral groove, starting below the junction of the splenic with the mesenteric vein and ending above it, making two complete clockwise turns. In life this can be seen as a band of thickening in the vein wall, the wall bulging between the turns of the spiral. Within the vein the band of thickening corresponds to a flap or ridge projecting from the vein wall, composed of a fold in the intima and media, bridged by a continuous adventitial coat.

This structure was present in all of twelve rabbits examined. Its occurrence in other species is being investigated. Preliminary observations suggest that it is present in other small rodents but not in dogs or man.

If, as seems likely, this structure rotates the portal blood stream within the vein, then the speed of rotation will vary with flow-rate and the distribution of the different components of the portal blood to the efferent branches of the vein will vary. Since minor fluctuations in flow-rate probably occur with the respiratory changes in intra-abdominal pressure, the final result may be randomization of the distribution within the liver of the blood from any given tributary.

The presence or absence of such a spiral fold within the portal vein of any species is clearly of great importance in assessing the probability of selective distribution of the portal blood within the liver of that species.

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Life-History of *Phyllodistomum simile* Nybelin

It is of interest to note that although sixty-one species of *Phyllodistomum* have been described, the life-cycles of only four have been determined experimentally and recorded. All four are American species. In Europe, however, no successful experimental work has been undertaken, although several early workers including Sinitsin[1], Reuss[2], Odhner[3], and Nybelin[4] have postulated, on the basis of morphological similarities, certain relationships between cercariæ, metacercariæ and sexually mature phyllodistomes. Many of the suggestions made in this connexion were contradictory.

The purpose of this communication is to place on record that the life-history of *P. simile*, a European species, has been elucidated by me under experimental conditions. The trematode was found in the urinary bladder of brown trout, *Salmo trutta* L., taken from the River Teify in mid-Wales. This appears to be the first record of *P. simile* in Britain. The tubular, motionless, sporocyst stages occurred in the epibranchial cavity and between the gill lamellæ of *Sphaerium corneum* L. The cercariæ are liberated from the daughter sporocysts through the birth pores and, after entering the epibranchial cavity of the clam, emerge to the outside through the exhalent siphon. The cercaria is of the macrocercous type, with a cercarial chamber in the tail, into which the body of the cercaria is completely retracted. It possesses a stylet, six pairs of penetration gland cells and a flame-cell formula of $2(4+4)+(4+4+4+4)$. There is no pharynx.

Attempts to infect aquatic insects and minnows, *Phoxinus phoxinus* L., were unsuccessful. Brown trout, *Salmo trutta* L., known to be free from infection, were, on the other hand, successfully infected in the laboratory with metacercariæ which had encysted precociously in the daughter sporocysts. Sexually mature worms were recovered three months after the initial infection. It is noteworthy that while the cercaria and certain aspects of the life-history differ from those described by the European workers, they bear many resemblances to those of the American species described by Beilfuss[5]. A detailed description of the cercaria and the life-history will be published elsewhere.

I am indebted to the Department of Scientific and Industrial Research for financial help, and also to Mr. L. E. Hughes, of the Veterinary Investigation Laboratories, Aberystwyth, for undertaking the experimental infection of the trout.

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Meiosis without Chiasmata in *Periplaneta americana*

That meiosis in *Periplaneta americana* is characterized by the absence of any visible chiasma has already been reported by Morse[1] and Suomalainen[2]. However, this absence of visible chiasmata with the consequent parallel disposition of the homologues in the bivalents from the zygotene to the pro-metaphase I, in this species, differs from that in coccids[3] and dragon-flies[4], but resembles *Callimantis*[5] inasmuch as the meiosis is pre-reductional. A thorough examination of the chromosomes during the prophase of the first meiotic division reveals that this anomalous type of meiosis is closely related to the persistence of the single thread of each homologue right from the leptotene to the pro-metaphase, and it is only during the pro-metaphase stage, which is of a little longer duration than usual, that the latter is duplicated. In fact there is very little difference between the bivalents at the late zygotene and those at the early pro-metaphase, and it is the orientation of the bivalents at the metaphase plate which results in the regular segregation (pre-reduction) during anaphase of the first division. Thus, like *Callimantis*, the diplotene and diakinesis which are of practically universal occurrence in the typical pre-reduction meiosis are altogether absent in this species.

This anomaly of meiosis in *P. americana* does not, however, go in any way against the precocity theory of Darlington[6]. The homologous chromosomes in each bivalent are held together by the force of attraction due to the singleness of each homologue, even in the absence of any chiasma, throughout the prophase of the first meiotic division. The regular disposition of the bivalents at the metaphase is, however, partly due to the repulsion of the homologues, because of their duplication and partly by their orientation, which is, perhaps, accompanied by some sort of poleward pull of the homologous centromeres towards the opposite centrosomes. Unlike *Callimantis*, therefore, where according to Hughes-Schrader[5] the two pairs of chromatids show no repulsion except at the kinetochores, the repulsion of mainly the homologues, in this species, appears to

play the major part in the formation of metaphase bivalents, as is evident by the ring-like configurations at this stage. The kinetochores do not appear to show any repulsion whatever, at least in some of the bivalents. In fact the homologues of each bivalent appear to be held together, at the metaphase, by the residual affinity or the terminal attraction even in the absence of any chiasma.

A detailed account of the structure and behaviour of the chromosomes in *P. americana* will shortly be published elsewhere.

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Crossing-over in *Drosophila willistoni*

In the course of analysing the frequency of chromosomal inversions in 292 adult females of *Drosophila willistoni*, we have recorded for the first time evidence of crossing-over between two non-overlapping inversions in the same chromosome arm of this species. These findings are of some general interest since, as Dobzhansky and Epling[1] have said: "The biological function of inversions in natural populations of *Drosophila* and their principal role in the evolution of these insects might be conceived to be the suppression of crossing over between gene complexes which have reached an adaptive equilibrium. Crossing over would destroy these complexes and would result in gene combinations of different adaptive values, but would be prevented by the binding effect of the inversions".

In *D. pseudo-obscura* Dobzhansky and Epling found a strong suppression of crossing-over in the third chromosome due to inversion heterozygosis. Such suppression of crossing-over is adaptive, for the reasons Dobzhansky and Epling give. At the same time suppression of crossing-over reduces one source of genetic plasticity. However, there is gain in plasticity in other ways since crossing-over appears to be intensified on those chromosomes without inversions in individuals heterozygous for inversions on a given chromosome. This is true of *D. pseudo-obscura* as well as of other species[1]. In *D. willistoni* the inversions occur on all chromosomes. Suppression of crossing-over on all chromosomes would then cause a great reduction in genetic plasticity. But this does not seem to occur, as the following results indicate.

We have examined the frequency of inversion heterozygotes of six offspring of each of 292 crosses of wild virgin females with males of a strain homozygous for its gene arrangements. Table 1 shows the minimal frequency with which crossing-over occurred between inversions *B* and *J* on the third chromosome and between inversions *E* and *F* on the left arm of the second chromosome. These are minimal frequencies since not all crossing-over will be recorded in this way. There were insufficient numbers of pairs of heterozygous inversions on the other chromosomes for us to obtain estimates for these chromosomes. The flies were bred from three different wild fruits. There are no significant differences between the fruits, so the samples may be regarded as replicates. For chromosome *IIL* the minimal mean frequency of crossing-over between inversions *E* and *F* was 19·7. This is remarkably high as these two inversions are quite close to one another on the chromosome. For chromosome *III* the mean frequency of crossing-over between inversions *B* and *J* was 11·7. This is less remarkable as the distance between these two inversions is quite large, *B* being at the base of the chromosomes and *J* near the tip.

Table 1. Minimal estimates for the frequency (per cent) of crossing-over between inversions *E* and *F* in the left arm of the second chromosome and between inversions *B* and *J* in the third chromosome of *Drosophila willistoni*. Flies were bred from three different fruits

Fruit	Chromosome and inversion		No. of flies
	IIL *E* and *F*	*III* *B* and *J*	
Philodendron sp.	23	9	100
Psidium araça	20	11	100
Arecastrum romanzoffianum	16	15	92
Mean	19·7	11·7	

These high frequencies of crossing-over in *D. willistoni* are quite in conformity with the principle formulated by Dobzhansky and Epling[1] to which we have already referred. It is what might be expected to happen in a species in which inversions are spread through all the chromosomes. The inversions maintain the integrity of blocks of genes within the inversions but do not inhibit recombination as between inversions.

Bruno Battaglia
L. C. Birch

Institute of Zoology,
University of Padua;
Department of Zoology,
University of Sydney;
Department of General Biology,
University of São Paulo,
Brazil.

[1] Dobzhansky, Th., and Epling, Carl, *Proc. U.S. Nat. Acad. Sci.*, **34**, 137 (1948).
[2] Da Cunha, A. B., *Adv. in Gen.*, **7**, 93 (1955).

Chromosomes of the Cultivated Mushroom

Since the original work by Maire[1], the attention of a number of cytologists[2–4] has been attracted to the study of nuclear behaviour and basidiospore formation in the two-spored cultivated mushroom, *Agaricus campestris* Fr. var. *bisporus*[5]. Sass[2] first published a full account of meiosis in the basidium, and although in one of his diagrams eight bivalents are clearly figured he reported a diploid chromosome number of approximately eight, a determination which was later confirmed[4]. In the interim, however, Colson[3], after a most comprehensive study, reported a chromosome number of $n=9$.

The results of an investigation using a variety of mushroom grown on a commercial scale in Great Britain have proved of considerable interest, and a chromosome number differing from the two earlier recorded numbers has been found. In this material,

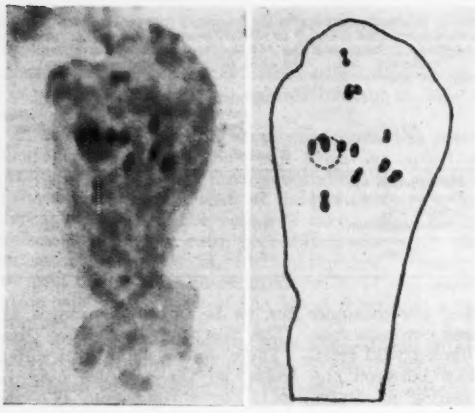

Fig. 1. Metaphase I showing twelve bivalents and a persistent nucleolus. Note the small bivalent in the 11 o'clock position (× 2,860)

twelve chromosomes have been observed at mitosis, and twelve bivalents are regularly formed at meiosis (Fig. 1). The chromosomes are extremely small and at metaphase I of meiosis the largest bivalent is slightly more than 1μ long.

Possible explanations for the reported differences in chromosome number are: (1) that different strains of the fungus having different chromosome numbers have been studied (the two haploid numbers of four were determined from American and French material, whereas the two higher counts were found in British material); or (2) that differences in chromosome number are due to limitations of technique.

In the Autobasidiomycetes, haploid chromosome numbers of $n=4$ are most common[6], the haploid number of twelve for the mushroom being the highest reported in this group. The possibility that the variety studied is triploid has been investigated, but evidence indicative of a polyploid origin has not been found; meiotic pairing is complete and no multivalent associations have been observed.

The second possibility, that differences in chromosome number are due to inadequacy of techniques, is suggested because all earlier work was carried out using sectioned material. In the present work, considerable use was made of sectioning techniques; but it was found that reliable chromosome counts could not be obtained with such methods. The chromosomes contain considerable amounts of heterochromatin, and in many of the preparations studied there was a tendency for secondary association of bivalents. Associations of bivalent chromosomes are difficult to resolve in sectioned material, and consistently accurate counts were only achieved through the use of squash techniques. For this purpose, material was fixed in a mixture of chloroform, ethanol and glacial acetic acid (7 : 5 : 2) and stained in aceto-carmine or acetic orcein.

Although the possibility of the existence of different chromosome races cannot be ruled out, the minuteness of the chromosomes, together with the inadequacy of sectioning methods for accurate chromosome analysis, lend support to the suggestion that previous counts may have erred on the low side.

This work was conducted in the Department of Agricultural Botany, Aberystwyth, under the direction of Prof. P. T. Thomas, whose help and encouragement are gratefully acknowledged: a more detailed account will be published later.

H. J. Evans

Medical Research Council Radiobiological Unit,
Atomic Energy Research Establishment,
Harwell, Berks.

Aug. 1.

[1] Maire, R., *Bull. Soc. Mycol. France*, **18**, Supp., 1 (1902).
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[3] Colson, B., *Ann. Bot.*, **49**, 193 (1935).
[4] Sarazin, A., *C.R. Acad. Sci., Paris*, **206**, 275 (1938).
[5] Kligman, A. M., *Amer. J. Bot.*, **30**, 745 (1943).
[6] Olive, S. L., *Bot. Rev.*, **19**, 439 (1953).

Dormancy of Seeds of *Phalaris arundinacea* and *Phalaris tuberosa*

Dormancy, giving rise to irregular and poor germination, is a characteristic of certain strains of *Phalaris arundinacea* and *P. tuberosa*.

Seeds of the Welsh Plant Breeding Station strain *S.*230, a hexaploid hybrid derived from *P. tuberosa* × *P. arundinacea*, were subjected to thirteen treatments, as in Table 1, and incubated on a Jacobsen apparatus at 25° C. with access to light. Seeds of a commercial strain of *Lolium perenne* were used as a check.

The treatments involving dehulling, scarifying and pricking show a significant increase in germination compared with the control. The causal factor of dormancy remains unknown; but the following points are indicative: (1) The caryopses swell, therefore water is not limiting. (2) Pricking the palea with a pin and scarifying are partially effective, therefore a chemical inhibitor within the palea is unlikely, and this is borne out by the ineffectiveness of the soil and water treatments designed to reduce the concentration of a possible inhibitor. (3) Pricking can be effective, so mechanical impedance of the coleorhiza by the palea is unlikely, particularly as seeds dehulled after twenty-one days incubation showed no signs of rupture of the integument. (4) Treatments designed to remove epidermal secretions of wax, fat, etc., failed to have any significant effect on germination, though possibly they were not sufficiently drastic. (5) After twenty-one days incubation the palea were removed from a number of seeds within each treatment which had failed to germinate, and within 48 hr. a high percentage (30–100 per cent) had emerged.

Table 1. The Germination Percentage of *S.*230 when subjected to Various Treatments

Treatment \ Time	No. of days				
	3	5	7	14	21
Acetone for 15 sec.	0	0·41	0·41	0·82	1·23
Acetone for 3 min.	0	0·79	0·79	1·2	1·2
50° C. water for 5 min.	0	0	2·9	3·9	4·5
50° C. water for 20 min.	0	0	1·6	2·8	3·6
4*N* sulphuric acid for 60 sec.	0	0·4	1·2	2·2	3·2
Ether for 15 sec.	0	2·2	2·4	4·4	5·2
70 per cent ethyl alcohol for 15 sec.	0	0·4	1·6	2·6	2·8
Germinated in 4 mm. deep tap water	0	0·4	1·2	1·4	1·6
Germinated on moist garden soil	0	0	1·2	1·2	3·6
Germinated on washed soil	0	0	1·2	2·4	2·8
Pricked with a pin	11·1	19·7	26·7	32·7	37·4
Scarified with sand paper	14·8	35·4	42·5	48·3	50·9
Dehulled	41·9	63·4	70·9	73·1	73·1
Control	0	1·2	2·8	3·4	4·8
Commercial *Lolium perenne*	36·3	84·8	88·8	90·8	90·8

A gaseous inhibitor is not inconsistent with the above facts, and it is suggested that failure to germinate is due either to a lack of oxygen, or to a build-up of carbon dioxide concentration having a narcotic effect, within the immediate region of the germinating embryo.

A more detailed report of this and other experiments will appear elsewhere.

P. B. Vose

Welsh Plant Breeding Station,
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July 25.

Differences in Social Aggregation in Two Species of Locust

Natural populations of locusts are characterized by large fluctuations in numbers, accompanied by changes in morphology, colour and behaviour in both the nymphs (hoppers) and the adults. When numbers are high, the hoppers aggregate into bands containing from a few hundred to several thousand individuals. Similar gregarious hoppers can be produced in the laboratory by rearing several together in one cage[1]. There is much circumstantial evidence to suggest that, provided the total numbers are sufficient, the formation of hopper bands depends partly on a patchy physical environment, especially a vegetation mosaic, and partly on strong attractions between hoppers[2,3].

In the laboratory, the hopper inter-attractions leading to aggregation have been studied in cages that provide a physically uniform environment[4]. In recent experiments, groups of ten hoppers were tested in an evenly lighted and heated, ring-shaped cage, the floor of which was marked radially into twenty equal divisions. When first placed in the cage, the ten hoppers moved about; but later they settled down, those in the same division generally touching one another. After 30 min. the number in each division was noted. The hoppers were then disturbed so that the groups were broken up, and after another 30-min. period the number in each division was again noted. Four such readings constituted a test. No hopper group was subjected to more than one test per day.

If the hoppers settled at random, the number of cage divisions containing 0, 1, 2, 3, and so on, would follow a binomial distribution given by the formula $(19/20 \times 1/20)^{10}$. The percentage of hoppers grouped (that is, in groups of two or more) would be 37·5, and in each test of four readings, involving 80 divisions, 48 divisions would be empty, 25 would contain one hopper and 7 would contain two or more. If more hoppers were grouped than one would expect for random distribution, then the grouping was due to the hoppers being attracted to one another, since the cage provided a physically uniform environment and the hoppers moved actively before coming to rest. Such grouping has been called social aggregation[4]. In successive tests, any differences in the amount of grouping was a measure of the difference in strength of hopper inter-attractions.

Two locust species, *Locusta migratoria migratorioides* (R. and F.) and *Schistocerca gregaria* (Forsk.), were compared. They came from the routine stocks of the Anti-Locust Research Centre that have been kept crowded in cages for many generations. Small batches of hoppers (six batches of *Locusta* and seven of *Schistocerca*) were tested soon after hatching and at intervals of one or two days afterwards until the end of the first instar. The tests were carried out at an air temperature of 28° C. and the hoppers were well fed before each test, these physical conditions having been found to be optimal for social aggregation in both species[4,5].

Table 1. The Average Number of Divisions containing 0, 1, 2, 3 or more Hoppers
(The figures are based on 3–5 separate tests, each test consisting of four readings)

Age from hatching	*Locusta*					*Schistocerca*				
	No. of hoppers per division				P*	No. of hoppers per division				P*
	0	1	2	3 or more		0	1	2	3 or more	
Up to 3 hr.	47	27	5	1	>0·8	52	21	4	3	>0·5
6–12 hr.	53	19	6	2	>0·3	55	15	6	4	<0·05
1 day	52	20	6	2	>0·3	58	13	4	5	<0·02
2 days	55	16	4	5	>0·05	58	12	6	4	<0·01
3 days	58	12	5	5	<0·01	59	13	2	6	<0·02
4 days	58	13	5	4	<0·02	58	13	4	5	<0·02
5 days (near to moulting)	55	15	6	4	<0·05	55	15	6	4	<0·05

* Probability of distribution being random

Soon after hatching and the intermediate moult, when the cuticle was still a little soft, the hoppers of both species distributed themselves at random within the cage (Table 1). About six hours after hatching, the *Schistocerca* hoppers showed strong attractions for one another and their distribution was probably not a chance one. One day after hatching, *Schistocerca* showed maximum social aggregation and the hopper distribution differed significantly from chance. This contrasted strongly with the behaviour of the *Locusta* hoppers, which continued to settle at random until they were two or three days old, maximum aggregation not occurring until they were three or more days old.

The hatching of hoppers of swarming populations of *Schistocerca* has often been observed in the field. The hoppers of each egg pod usually hatch within a few minutes of one another[2] and the number from a single pod is generally between 40 and 90. Consequently, the hoppers begin their life by being grouped. For the first five or six hours after hatching they are very inactive and remain grouped around the egg-pod holes. If they are undisturbed, very little movement takes place during the first day. The laboratory experiments suggest that one day of grouping is sufficient for the hoppers to learn to aggregate and so to resist factors leading to dispersal. No corresponding field observations have yet been made with hatchlings of swarming populations of *Locusta*, but the specific difference in social aggregation demonstrated in the laboratory suggests that under natural conditions hatchlings of *Locusta* are more easily dispersed than those of *Schistocerca*. It also seems likely that a patchy physical environment is of greater importance in the retention of groups and the formation of new ones in *Locusta* than in *Schistocerca*.

I wish to thank Prof. G. C. Varley for laboratory facilities in the Hope Department, Oxford.

Peggy E. Ellis

Anti-Locust Research Centre,
London.
Aug. 17.

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[5] Ellis, P. E. (unpublished laboratory data).

"Lucubratory Biochemistry"

Under this title a review of my biochemistry text-book was published in *Nature* of March 24, p. 544. The reviewer criticizes many of my statements by expressions such as "astonishing dictum", "Paradox indeed", or by other ironical remarks. A reply to each of the numerous comments would occupy much space. Therefore, only a few of them can be answered here.

The reviewer quotes as "interesting" the statement that natural isotopes are stable, and asks: "Has Dr. Haurowitz never heard of naturally occurring radioactive isotopes, for example of potassium or of carbon?" It is not evident from the review that the statement criticized is made in a section on "Methods", in which only those isotopes are treated which are used as tracers in biochemical research. Obviously, the statement on the stability of natural isotopes applies only to isotopes of this type. Natural radioactive potassium and carbon, mentioned in the question of the reviewer, are not used as tracers. Potassium-42 and carbon-14, used in tracer work, are produced artificially. The obvious answer to the first part of the question asked by the reviewer is that every high-school boy knows about the occurrence of uranium and of other radioactive isotopes in Nature. One may wonder why the question was asked.

The review contains the following comment: "On p. 132 the statement is made, 'The amino acids are colorless substances that are soluble in water', although later the insolubility of cystine in water is mentioned (p. 156)". On p. 156 I wrote: "Cystine, in contrast to cysteine, is almost insoluble in water". Omission of the word "almost" creates here a contradiction.

Another comment refers to the following words of my book: "Attempts to prepare estrogenic hormones synthetically, led to the unexpected result that certain *stilbene derivatives*, such as dihydroxydiethylstilbene, are just as active as estradiol". This statement is criticized as "historically incorrect, as can be seen by consulting the early papers of Dodds and his collaborators". Dodds and his co-workers, in their paper on the œstrogenic activity of stilbene derivatives (*Proc. Roy. Soc.*, **127**, p. 140), wrote: ". . . in view of the difficulties presented by the total synthesis of the naturally occurring œstrogenic hormones, attempts were made to prepare more accessible substances the molecules of which would be similar to œstradiol in shape, weight and in the situation of the hydroxyl groups". Readers of *Nature* will now be able to judge whether my presentation was "historically incorrect".

More than a dozen examples of a similar type could be added. They would not show more than the three examples given above, namely, that most of the comments of the reviewer are hypercritical and that the text of my book is not so inadequate as it may appear to those who read only the review in *Nature*.

Felix Haurowitz

Department of Chemistry,
Indiana University,
Bloomington, Indiana.
Aug. 5.

Since my review was critical, I attempted to be as fair as possible by quoting at length some of the extracts with which I did not agree. I do not believe that any useful purpose can be served by arguing about individual points, although I could take up each of the comments which Prof. Haurowitz has made. I am content to leave those who wish to judge whether my review was fair or not to read it in relation to the book itself.

F. G. Young

Department of Biochemistry,
University of Cambridge.

A Word Common to the Natives of Alaska, Canada, Greenland and Brazil

Dr. Nicholas Polunin has suggested that I should direct the attention of botanists and others to the ancient provenance of a word which appears to mean fundamentally 'the juice of a plant that is used for chewing', as a chewing gum.

Not being English or French, but of speech a mid-west American from Manitoba and Dakota, it did not mean anything to me when in 1906 I heard the Eskimos of the Mackenzie Delta and north-eastern Alaska speaking of spruce gum as 'kutsuk'. They used to fetch this themselves from the evergreen forest to the south or buy it from the forest Indians; more recently, they had been buying flavoured chewing gum from the whalers, which they also spoke of as 'kutsuk', as they did of a substitute of their own, dried seal blood, which they said they "always" used in the pre-white days if they ran out of spruce gum for their children to chew.

Years later, perhaps in 1912, I learned that the word for the gum of a Brazilian plant, and of other South American plants, is 'caoutchouc', and the Oxford Dictionary defines it as "a milky resinous juice of certain trees in S. America . . .". The Oxford Dictionary goes on to connect the derivation of this word for rubber with a French expedition to the Amazon country in 1739. 'Webster' has the same tale, more briefly, and gives varied spellings, among them 'caucho' and 'gutteux'. I like the last best, for it is nearest to what I have heard among the Eskimos from Bering Strait to Coronation Gulf. They said 'gutsuk', the *s* as always in their tongue with an *sh*- sound.

Turning now to Greenland, in Sam. Kleinschmidt: "Den Grönlandske Ordbog" (Copenhagen, 1871), I find "kutsuk. (1) Harpix (det almindelege, af Naaletraeer; (2) hvad der paa samme Maade udsondrer sig i andre Traeer: Gummi, Campher og lignende producter". Schultz-Lorentsen's "Dictionary of the West Greenland Eskimo Language" (Copenhagen, 1927) has only: "kutsuk, resin, gum".

So we appear to have in the New World a term for the gum of a plant which people use for chewing and call by the same name from Greenland to Alaska to Brazil. When I first began to talk about this, I was told it was coincidence. But the intellectual climate is changing, among other things in linguistics, and now the disciples of men like Uhlenbeck and Hammerich think 'connexion' a likelier word than 'coincidence'. Incidentally, I found the Eskimos saying 'ignirk' for fire and I knew that the Romans said 'ignis'; but again my linguist friends said 'coincidence'; now I believe the followers of Uhlenbeck think we have in this a connexion from the Sanskrit to the Latin to the Eskimo.

Vilhjalmur Stefansson

Dartmouth College,
Baker Library,
Hanover, New Hampshire.

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 5

SOCIETY OF ENGINEERS (in the Apartments of the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. D. F. Collins: "Gas Turbines in Theory and Practice".

SOCIETY OF CHEMICAL INDUSTRY (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. T. V. Arden: "Recovery of Uranium from Low-grade Ores".

ROYAL INSTITUTE OF CHEMISTRY (at Norwood Technical College, Knights Hill, West Norwood), at 7 p.m.—Mr. E. N. Jenkins: "Laboratory Techniques in Radiochemistry".

Tuesday, November 6

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Prof. M. E. L. Mallowan: "Twenty-five Years of Mesopotamian Discovery".

INSTITUTION OF CIVIL ENGINEERS (at Great George Street, Westminster, London, S.W.1), at 5.30 p.m.—Mr. H. J. F. Gourley: Presidential Address.

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. E. H. Holt: "Electric Strength of Highly Compressed Gases"; Dr. P. R. Howard: "Insulation Properties of Compressed Electro-Negative Gases".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. W. A. Robson: "The Welfare State".* (Hobhouse Memorial Lecture.)

UNIVERSITY OF LONDON (in the Gustave Tuck Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. J. A. Ratcliffe: "The Ionosphere".* (Further lectures on November 13, 20 and 27.)

Wednesday, November 7

INSTITUTE OF PETROLEUM (at 26 Portland Place, London, W.1), at 3 p.m.—Symposium on "Digital Computers in the Petroleum Industry".

INSTITUTION OF CHEMICAL ENGINEERS (at the Royal Institution, Albemarle Street, London, W.1), at 3 p.m.—Symposium on "Grinding".

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1), at 5.15 p.m.—Symposium on "The Spectral Approach to Time Series". Papers by Mr. A. M. Walker, Mr. S. K. Zaremba and Mr. Z. A. Lomnicki and Dr. P. Whittle.

SOCIETY FOR ANALYTICAL CHEMISTRY (in the Meeting Room of the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Dr. H. M. N. H. Irving: "The Structure of Dithizone and its Metal Complexes".

Thursday, November 8

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. M. Blackman and Mr. N. D. Lisgarten: "The Cubic and other Structural Forms of Ice at Low Temperature and Pressure"; Mr. J. F. Nye: "The Distribution of Stress and Velocity in Glaciers and Ice Sheets".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. J. Eccles: Lecture on the Visit of the British Electricity Supply Delegation to the Soviet Union.

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. D. C. Broome and Mr. A. Please: "The Use of Mechanical Tests in the Design of Bituminous Road Surfacing Mixtures, Part 2—Stability Tests on Rolled Asphalt".

INSTITUTION OF MECHANICAL ENGINEERS, LUBRICATION AND EDUCATION GROUPS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6.45 p.m.—Discussion on "The Extent to which Lubrication should enter into First Degree and H.N.C. Courses".

ROYAL INSTITUTE OF CHEMISTRY (joint meeting with the ACTON TECHNICAL COLLEGE SCIENTIFIC SOCIETY, at Acton Technical College, High Street, Acton, London, W.3), at 7 p.m.—Prof. M. J. S. Dewar: "Some Aspects of Modern Theoretical Chemistry".

Friday, November 9

INSTITUTION OF MECHANICAL ENGINEERS, HYDRAULICS GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. E. H. Lever, Dr. H. Ritter, Mr. M. Woolfson and Mr. C. T. Wright: "Rotating Beam Channel and 30-in. Water Tunnel at the Admiralty Research Laboratory".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. A. Renfrew: "Plastics in Perspective".* (Fifth of ten University Extension Lectures on "Technology and Industry". Further lectures on November 16, 23, 30, December 7 and 14.)

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (in the Chemistry Lecture Theatre, King's College, Strand, London, W.C.2), at 7 p.m.—Dr. F. Sanger: "The Chemistry of Insulin".

ROYAL INSTITUTION (at 21 Albermarle Street, London, W.1), at 9 p.m.—Prof. Sir Charles Dodds, F.R.S.: "The Chemical Substances Influencing Mental and Physical Development".

Friday, November 9—Saturday, November 10

BRITISH SOCIETY FOR IMMUNOLOGY (at the Wellcome Foundation, 183 Euston Road, London, N.W.1), at 10 a.m.—Scientific Papers. Friday afternoon—Symposium on "Complement".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

BIOLOGIST (with a degree in biochemistry or physiology) to the Hospital and Medical School—The Secretary, King's College Hospital Medical School, Denmark Hill, London, S.E.5 (November 9).

ASSISTANT, Grade B, IN PHYSICS—The Clerk to the Governors, Woolwich Polytechnic, London, S.E.18 (November 10).

SCIENTIST (with a good degree (preferably in chemistry) or equivalent qualification, and preferably previous editorial experience), for duties which include the progressing of research programmes, editing research reports, etc.—The National Coal Board, Coal Research Establishment, Stoke Orchard, near Cheltenham, Glos, quoting X.450 (November 12).

PASTURE RESEARCH OFFICERS (3) (either with a degree in the natural sciences, with botany as a major subject, and postgraduate training in ecology and pasture research, or a degree in agriculture with training in pasture research, and preferably with experience in the establishment and management of pastures and in the management of dairy cattle and sheep) IN THE DEPARTMENT OF RESEARCH AND SPECIALIST SERVICES, Federal Ministry of Agriculture, Federation of Rhodesia and Nyasaland—The Public Service Attaché, Rhodesia House, 429 Strand, London, W.C.2 (November 15).

HOSPITAL BIOCHEMIST, Senior or Principal Grade (with a university degree in science or equivalent qualification, and preferably with a higher qualification or good research experience), in the routine Biochemical Laboratory—The House Governor and Secretary, Royal Victoria Infirmary, Newcastle-upon-Tyne 1 (November 17).

LECTURER IN PSYCHOLOGY in St. Salvator's College—Joint Clerk to the University Court, College Gate, St. Andrews (November 17).

PHYSICAL CHEMISTS and CHEMICAL ENGINEERS (with a good honours degree or equivalent, and preferably experience), for important technical research into developing new processes for making smokeless fuels—The National Coal Board, Coal Research Establishment, Stoke Orchard, near Cheltenham, Glos, marking envelope "X/447" (November 19).

ASSISTANT LECTURER IN ZOOLOGY—The Secretary, The Queen's University, Belfast (November 20).

SENIOR LECTURER, LECTURER or ASSISTANT LECTURER IN BOTANY at the University, Khartoum—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 20).

LECTURER (British subject, with a first- or second-class honours degree in mathematics, and preferably teaching experience) IN THE DEPARTMENT OF MATHEMATICS—The Director of Studies, Royal Naval College, Greenwich, London, S.E.10 (November 24).

LECTURER (with special qualifications in palæontology) IN GEOLOGY—The Registrar, King's College, Strand, London, W.C.2 (November 24).

ASSISTANT IN INORGANIC OR PHYSICAL CHEMISTRY—Joint Clerk to the University Court, Queen's College, Dundee (November 30).

CHAIR OF GEOLOGY in the University of Khartoum—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 30).

LECTURER or ASSISTANT LECTURER IN MATHEMATICS at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, November 30).

LECTURER (with a degree or diploma and preferably research, teaching and industrial experience) IN GENERAL CHEMISTRY FOR ENGINEERING STUDENTS in the School of Applied Chemistry, New South Wales University of Technology, Sydney, Australia—The Agent General for New South Wales, 56 Strand, London, W.C.2 (Australia, November 30).

UNIVERSITY LECTURER IN MATHEMATICS—The Secretary, Appointments Committee of the Faculty of Mathematics, The Arts School, Bene't Street, Cambridge (November 30).

X-RAY CRYSTALLOGRAPHER (preferably with some experience of powder methods and work on metals), for special investigation sponsored by the Central Electricity Authority—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (December 1).

CHAIR OF CHEMISTRY—The Secretary and Registrar, The University, Southampton (December 15).

SENIOR PHYSICIST (with a B.Sc. degree, preferably with honours in physics, and an extensive knowledge of electronics) with the Auckland Hospital Board, New Zealand, for duties which include responsibility for a 4 MeV. linear accelerator—Office of the High Commissioner for New Zealand, 415 Strand, London, W.C.2 (New Zealand, December 31).

BIOLOGIST (with a biological degree with emphasis on botanical and biochemical subjects) to carry out an investigation into the nature of the food of British wildfowl and into the nutritional requirements of wildfowl in captivity—The Assistant Director (Research), The Wildfowl Trust, Slimbridge, Gloucestershire.

CHEMIST (with an honours degree or A.R.I.C. or F.R.I.C., and at least three years post-qualification experience) IN THE MEDICAL DEPARTMENT, Government of Hong Kong—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.117/51/018.

ENGINEER or PHYSICIST (young graduate, preferably with some mathematical ability and experience in the use of electronic instruments) at Sheffield, for work on the problems of file testing and manufacture—The Personnel Officer, British Iron and Steel Research Association, 11 Park Lane, London, W.1, quoting "F.2".

EXPERIMENTAL OFFICER/ASSISTANT EXPERIMENTAL OFFICER (with at least H.N.C. chemistry or equivalent), to assist in fundamental and applied investigations relating to radioisotopes and surfaces—The

Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berkshire, quoting Ref. A.1154/34.

Experimental Officer (at least 26 years of age, with higher school certificate, or equivalent qualification, in science subjects) with the Technological Irradiation Group of the Isotope Division, to be responsible for the operation of a number of kilocurie radiation sources, and projects associated with the investigation of the effects of radiation on chemical reactions, foods and other materials—The Establishment Officer, Atomic Energy Research Establishment, Harwell, Didcot, Berks, quoting 661/34.

Laboratory Technician (qualified in biochemistry or chemical pathology) in the Department of Chemical Pathology—The Finance Officer, St. Thomas's Hospital Medical School, London, S.E.1.

Meteorologist (well qualified and experienced) with the Government of Cyprus, to investigate meteorological stations and the needs of technical departments concerned for climatological research; to advise on measures needed for reorganization, and to train a suitable Cypriot officer as his successor—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.57/17/01.

Physicist/Chemist (male or female, M.Sc. or B.Sc. (Hons.) with majors in chemistry and physics, and a knowledge of microscopy) in the Mines Department, Government of Northern Rhodesia, to undertake research into the problems of silicosis, particularly in connexion with analysis of mine-dust samples by X-ray diffraction and by chemical methods, and to set up and equip a laboratory at the Headquarters of the Mines Department in Northern Nigeria—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.99/3/04.

Research Fellow (with a degree in either physics, chemistry or metallurgy) in the field of the Viscosity of Molten Metals—The Department of Industrial Metallurgy, The University, Edgbaston, Birmingham 15.

Science Graduate (preferably with experience in clinical biochemistry), to work on metabolic studies at the Institute of Orthopædics, Royal National Orthopædic Hospital, Stanmore, Middlesex—The Dean, Institute of Orthopædics, 234 Great Portland Street, London, W.1.

Scientific Officer (with a good honours degree and an interest in biological problems, and preferably some research experience) in the Chemistry Department to take part initially in researches on the chemistry of the milk proteins and enzymes—The Secretary, National Institute for Research in Dairying, Shinfield, Reading, quoting Ref. 56/12.

Senior Lecturer or Lecturer in Mathematics; Senior Lecturers or Lecturers in Radar and Telecommunications; and a Senior Lecturer or Lecturer in Engineering Physics at the Royal Military College of Science, Shrivenham—The Ministry of Labour and National Service, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.361/6A.

Senior Lecturer (with a higher degree or considerable practical or research experience) in Civil Engineering with either hydraulics, hydrology or public health engineering—The Secretary, Royal College of Science and Technology, Glasgow, C.1.

Soil Analyst (with a good honours degree in chemistry and not less than three years postgraduate experience in soil or agricultural chemistry) in the Department of Soil and Land-Use Survey, Gold Coast Local Civil Service, to supervise routine analysis of soil samples; to carry out special soil analysis and laboratory investigations relating particularly to the nutrient status of soils used for cocoa production, and to undertake the training of junior analytical assistants—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.79/13/06.

Soil Scientist (with an honours degree in natural science, chemistry and/or botany) in Gambia (H.M. Oversea Civil Service), to undertake research into soil deficiencies—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/12/010.

Technician (male or female, preferably with research experience) in the Department of Pharmacology—The Secretary, St. Mary's Hospital Medical School, Paddington, London, W.2.

Zoologist (with a good honours degree in zoology and preferably the ability to pilot light aircraft) to assist in the study of the populations and ecology of wildfowl—The Assistant Director (Research), The Wildfowl Trust, Slimbridge, Gloucestershire.

REPORTS and other PUBLICATIONS

(not included in the month by Books Supplement)

Great Britain and Ireland

Department of Scientific and Industrial Research: Road Research Laboratory. Road Research Technical Paper No. 36: The Sampling and Analysis of Rolled Asphalt and Coated Macadam. By C. M. Hough. Pp. vi+30+3 plates. (London: H.M. Stationery Office, 1956.) 3s. net. [238

1956 Supplement to *British Chemicals and their Manufacturers*. (The Directory of the Association of British Chemical Manufacturers.) Pp. 35. (London: Association of British Chemical Manufacturers, 1956.) [238

Ministry of Housing and Local Government and Scottish Office. The Surface Water Year-Book of Great Britain, 1953–54: Hydraulic Statistics for British Rivers together with related Rainfalls, for the year ended 30th September, 1954. Pp. xiii+117. (London: H.M. Stationery Office, 1956.) 30s. net. [238

Ministry of Agriculture, Fisheries and Food. Domestic Food Consumption and Expenditure, 1954: Annual Report of the National Food Survey Committee. Pp. v+89. (London: H.M. Stationery Office, 1956.) 5s. net. [238

National Union of Journalists. Freelance Directory, 1956. Pp. 1+66. (London: National Union of Journalists, 1956.) [238

Department of Scientific and Industrial Research. Report of the Building Research Board with the Report of the Director of Building Research for the year 1955. Pp. iv+72+16 plates. (London: H.M. Stationery Office, 1956.) 5s. net. [238

Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. No. 668, Vol. 240 (23 August 1956): The Layered Ultrabasic Rocks of Rhum, Inner Hebrides. By G. M. Brown. Pp. 1–53+5 plates. 27s. No. 669, Vol. 240 (23 August 1956): Properties of a Mass of Cells Capable of Regenerating Pulses. By R. L. Beurle. Pp. 55–94. 12s. 6d. (London: Royal Society, 1956.) [238

Land Utilization Map of Cyprus. (Bude and London: Geographical Publications, Ltd., 1956. Published for the World Land Use Survey.) 3s. [119

Single Story Industrial Buildings. Pp. 44. (London: Cement and Concrete Association, 1956.) [189

The Renaissance of Inorganic Chemistry. By Prof. R. S. Nyholm. (An Inaugural Lecture delivered at University College, London, 1 March 1956.) Pp. 24. (London: H. K. Lewis and Co., Ltd., 1956.) 2s. 6d. net. [189

Other Countries

The Written Word in Agricultural Advisory Work. Pp. 78. (Paris: Organisation for European Economic Co-operation; London: H.M. Stationery Office, 1956.) 450 francs; 9s.; 1.50 dollars. [238

Acta Universitatis Debreceniensis de Ludovico Kossuth Nominatae. Tom. 1, 1954. Pp. 206. (Budapest: Tankönyvkiadó, 1954.) [238

Bibliographie des Articles Parus dans les Périodiques Turcs, 1952. Index des noms d'Auteurs. Pp. 53. (Publication de l'Institut National Turc de Bibliographie.) (Istanbul: Maarid Basimevi, 1956.) [238

Atvinnudeild Háskólans: Fiskideild. Fjölrit Fiskideildar Nr. 6: Astand Sjávar á Síldeveidiavaedinu Nordanlands Sumarid 1955. By Unnsteinn Stefánsson. (Hydrographic Conditions on the North Icelandic Herring Grounds during the Summer, 1955. With an English Summary.) Pp. ii+23. Fjölrit Fiskideildar, Nr. 7: Rannsoknir á Atu, Hitastigi og Dreifingu Síldar Gerdar á Rannsóknaskipinu "Aegi" Sumarid 1955. By Hermann Einarsson. (Observations on Plankton, Temperature and the Distribution of Herring, made from the research vessel "Aegir", during the Summer of 1955. With an English Summary.) Pp. ii+21+7 plates. (Reykjavik: Atvinnudeild Háskólans: Fiskideild, 1956.) [238

Australian Map of Antarctica. Second edition, revised. (Canberra: Antarctic Division, Department of External Affairs, 1956.) [238

The Carlsberg Foundation's Oceanographical Expedition Round the World, 1928–30, and previous "Dana" Expeditions. Dana Report No. 42: The Miripinnati—a New Order of Teleost Fishes. By E. Bertelsen and N. B. Marshall. Pp. 34+1 plate. (Copenhagen: Andr. Fred. Høst and Son, 1956.) 10 Kr. [238

East Africa High Commission. Annual Report of the East African Council for Medical Research, 1954–1955. Pp. ii+40. (Nairobi: East African Council of Medical Research, 1956.) [238

National Academy of Sciences—National Research Council. Ninth Annual Report of the Pacific Science Board, 1955. Pp. 58. (Washington, D.C.: National Academy of Sciences—National Research Council, 1956.) [189

Fiskeridirektoratets Skrifter. Serie Havundersøkelser. Vol. 11, No. 5: Theragra Finnmarchica N.SP. Gadus Poutassou, Risso; Raia Spinicauda, Jensen. Eumicrotremus Spinosus Subspec. Nov. Eggvinii. Av Einar Koefoed. Pp. 24+3 plates. Vol. 11, No. 6: Cod Populations Identified by a Chemical Method. By Eva Henly Dannevig. Pp. 13. (Bergen: A/S John Griegs Boktrykkeri, 1956.) [189

Biologische Bundesanstalt für Land- und Forstwirtschaft in Berlin-Dahlem. Bibliographie der Pflanzenschutz-Literatur (Bibliography of Plant Protection), 1950. Bearbeitet von Dr. J. Bärner. Pp. xlii+438. (Berlin: Biologische Bundesanstalt für Land- und Forstwirtschaft, 1956.) [189

Bulletin of the Museum of Comparative Zoology at Harvard College. Vol. 114, No. 7: Post-Triassic Nautiloid Genera. By Bernhard Kummel. Pp. 321–494+28 plates. (Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1956.) [189

World Health Organization. Venereal Diseases: a Survey of Existing Legislation. Pp. 44. (Originally published in the International Digest of Health Legislation, 1956, 7, 155–198.) 2 Swiss francs; 3s. 6d.; 0.70 dollars. The Training of Sanitary Engineers: Schools and Programmes in Europe and in the United States. By Milivoj Petrik. (World Health Organization Monograph Series, No. 32.) Pp. 151. 12 Swiss francs; 20s.; 4 dollars. (Geneva: World Health Organization; London: H.M. Stationery Office, 1956.) [189

World Health Organization. Technical Report Series. No. 105: Expert Committee on Psychiatric Nursing—First Report. Pp. 43. 1 Swiss franc; 1s. 9d.; 0.30 dollars. No. 107: Joint FAO/WHO Conference on Food Additives, Geneva, 19–22 September 1955—Report. Pp. 14. 1 Swiss franc; 1s. 9d.; 0.30 dollars. No. 108: Expert Committee on Biological Standardization—Ninth Report. Pp. 20. 1 Swiss franc; 1s. 9d.; 0.30 dollars. (Geneva: World Health Organization; London: H.M. Stationery Office, 1956.) [189

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